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(54) Title: METHODS AND DEVICES FOR INHIBITING HAIR GROWTH AND RELATED SKIN TREATMENTS (57) Abstract <p>Methods of applying laser light to the skin, and apparatus therefor, include methods for removing hair, for synchronizing hair growth, for stimulating hair growth, for treating Herpes virus, for reducing sweat and body odor, for <i>in situ</i> formation of a chromophore in hair ducts, for reducing light loss at the skin surface, for grafting of hair stem cells, and for removing keloid or hypertrophic scars. The hair removal methods include controlling the proportions of photomechanical and photothermal damage by selection of laser parameters, chromophore particle size and/or pulse duration, with optional dynamic skin cooling. Additional hair removal methods include infiltrating a photoactivated drug into hair ducts and exposing the skin to sunlight or administering an anti-proliferative agent into hair ducts, for example, by encapsulating the anti-proliferative agent in a slow release vehicle. The methods of treating Herpes virus, reducing sweat or body odor, and removing keloid or hypertrophic scars include infiltrating a light-absorbing contaminant into hair ducts or other openings in the skin and illuminating the contaminated skin section. The methods for stimulating hair growth include grafting of cloned auto hair stem cells, the hair ducts or administering methionine to a skin section to increase hair growth. Apparatus useful in performing these methods include devices for making a smooth optical boundary between skin and air or for dividing a light beam into a plurality of smaller light beams, and dressings for use before, during and after laser illumination.</p>		

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METHODS AND DEVICES FOR INHIBITING HAIR GROWTH AND RELATED SKIN TREATMENTS

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation-in-part application of U.S. provisional application Serial No. 60/052,718, filed on July 16, 1997, and U.S. provisional application Serial No. 60/033,238 filed on December 5, 1996.

5 This application is related to co-pending U.S. patent applications Serial No. _____, filed October 21, 1997; Serial No. 08/777,576, filed December 31, 1996; Serial No. 08/695,200, filed August 1, 1996; Serial No. 08/644,231, filed May 13, 1996; Serial No. 08/492,283, filed June 19, 1995; Serial No. 08/489,358, filed June 12, 1995; Serial No. 08/489,352, filed June 12, 1995; and to U.S. application Serial No. _____, filed on
10 even date with this application, and which is incorporated herein by reference.

TECHNICAL FIELD

This invention relates to devices and methods for hair removal and skin treatments.

BACKGROUND

15 The known techniques of hair removal include electrolysis and various laser hair removal techniques and skin treatments. Laser hair removal is described in United States patents to Weissman *et al.*, U.S. Patent No. 4,388,924; Sutton, U.S. Patent No. 4,617,926; Mayer, U.S. Patent No. 3,538,919; and Zaias, U.S. Patent No. 5,059,192.

20 It is also known to effect long-term inhibition of hair growth by infiltrating a light-absorbing contaminant into hair ducts in a skin section prior to laser treatment. This technique is described in U.S. Patent Nos. 5,226,907 and 5,425,728 to Tankovich. A contaminant applied topically can also be used to facilitate laser skin resurfacing. The contaminant is infiltrated beneath the surface layers of the stratum corneum, and then the skin surface
25 bearing the contaminant is illuminated so as to remove the surface layers of the stratum corneum. This technique is described in U.S. Patent No. 5,423,803 to Tankovich.

Accordingly, after noting the limitations of the prior art techniques, the inventors of the present application have devised new methods and devices used in long term prevention of hair growth and other beneficial skin treatments.

SUMMARY

One embodiment of the invention is a method for inducing hairs in a section of skin into synchronized hair growth by applying a shock to hair follicles in the section of skin.

Another embodiment of the invention is a method for increasing the gradient of energy loss with depth in skin to assist in forcing contaminant particles into spaces in hair ducts and other skin structures. Devices for dividing a beam of light directed to a skin surface into a plurality of substantially smaller beams are useful for exerting a net downward vector on contaminant particles within hair ducts or other skin structures in the practice of the invention.

Another embodiment of the invention is a method for infiltrating a contaminant into hair ducts on a section of skin wherein the section of skin is covered with an occlusive dressing, such as a hydrogel, for long enough to cause spreading of the contaminant into the occluded hair ducts.

Another embodiment of the invention is a hydrogel dressing wherein an active agent beneficial for soothing or protecting irritated or inflamed skin is incorporated in a hydrogel matrix.

Another embodiment of the invention is a composite hydrogel for covering a skin surface during laser treatments. The hydrogel is scrimless and comprises a film of thermoplastic hydrogel joined along one face with a layer of cross-linked hydrogel polymer and a photoindicator that changes appearance upon irradiation with a laser beam.

Another embodiment of the invention is a method for controlling the proportions of mechanical and thermal damage caused to tissue surrounding hair ducts during hair removal procedures. One portion of the particles in a contaminant is selected to be large enough to explode upon illumination, and a second portion of particle is selected to be small enough to heat up without explosion upon illumination. The mechanical damage is proportional to the

portion of larger particles and the thermal damage is proportional to the smaller portion of particles in the contaminant.

Another embodiment of the invention is a method for providing any desired combination of photothermal and photomechanical damage to tissue surrounding hair ducts infiltrated with light absorbing particles. A skin section containing the hair ducts is illuminated with a
5 combination of long and short pulses of light absorbed by the particles, wherein the long pulses avoid explosion of a selected portion of the particles, thereby causing photothermal damage, and the short pulses explode or vaporize another portion of the particles, thereby causing photomechanical damage.

10 In another embodiment of the invention, growth of unwanted hairs in hair ducts in a section of skin is obtained by topically applying a sunlight-activated photochemical associated with microcarrier particles to a section of skin, allowing the microcarrier particles to penetrate into hair ducts, and bathing the treated section of skin in sunlight.

Another embodiment of the invention is a method for inhibiting hair growth by
15 applying an anti-proliferative agent to hair growth cells in a skin section so as to inhibit hair growth in the skin section.

In another embodiment of the invention, hair growth cells in hair ducts are contacted with a hair growth stimulating amount of methionine to stimulate hair growth in a section of skin.

20 Another embodiment of the invention is a method for preventing or treating outbreaks of a skin lesion due to reactivation of Herpes virus latent in hair ducts, wherein a contaminant is infiltrated into the hair ducts and the skin is illuminated by a light absorbed by the contaminant with consequent destruction of the Herpes virus in the hair ducts.

Another embodiment of the invention is a method for reducing production of sweat
25 and/or odor in which a light-absorbing contaminant is infiltrated into spaces in hair ducts adjacent to or within sweat glands, and the skin is illuminated with a light so as to transfer heat and kinetic energy from the contaminant to the tissue surrounding the sweat glands, thereby devitalizing the sweat glands and reducing or eliminating production of sweat in the treated skin section.

Another embodiment of the invention is a method for tailoring the treatment regimen and energy level used during laser hair removal treatment to accommodate such factors as an individual's hair and skin color, the depth of hair follicles at the anatomic location of the site to be treated, and any previous history of hair removal treatment.

5 Another embodiment of the invention is an improvement in a method for laser assisted hair removal wherein skin is irradiated with an illumination beam with a square or circular shape no wider than about 8.0 mm at its widest point.

Another embodiment of the invention is a method for *in situ* formation within hair ducts of a metal oxide useful as a light absorbing chromophore during laser-assisted skin
10 treatments.

Another embodiment of the invention is a method for reducing loss of light due to scattering and reflection of an incident light beam at a skin surface wherein the skin surface is covered with a transparent coating of liquid or a transparent device with a smooth upper surface for receiving an incident light beam. The covering has a refractive index slightly
15 greater than or equal to the refractive index of skin to minimize loss of energy from the incident beam.

Another embodiment of the invention is a method for stimulating hair growth in which an individual's healthy undifferentiated papilla and/or bulge area stem cells are harvested, cloned, and inoculated interdermally into a section of skin to stimulate hair growth
20 therein.

Another embodiment of the invention is a method for removal of hypertrophic or keloid scars wherein a scar is coated with a light absorbing contaminant and illuminated with short pulses of light preferentially absorbed by the contaminant for a time sufficient to selectively remove the scar.

25 Another embodiment of the invention is a method for inhibiting hair growth by filling hair ducts, from which hairs have optionally been removed, with a light guiding fluid, and, using a light well absorbed in blood chromophores, illuminating the section of skin containing the hair ducts so that at least a portion of the light is directed down the hair ducts by the fluid and absorbed in blood vessels that feed hair growth cells.

Another embodiment of the invention is a method for inhibiting hair growth by irradiating hair ducts infiltrated with light-absorbing contaminant particles, wherein the surface of a section of skin is precooled to about 10° C to -10°C prior to illumination, and a cooling flux is maintained on the surface of the skin section during a single laser pulse. The duration of the pulse is sufficient that tissue immediately surrounding the base of a hair follicle in the section of skin is destroyed by heat transferred from the irradiated contaminant. Meanwhile the cooling flux on the skin surface is sufficient that the temperature of tissue at a distance of about 1 to 2 hair follicle radii from the hair duct wall increases to no more than about 10° C above body temperature during the pulse. At the conclusion of the pulse, the cooling flux is terminated, and the surface of the section of skin is allowed to return to body temperature before the three-step process is repeated.

Another embodiment of the invention is a method for activating or retarding hair growth wherein a contaminant containing metallic particles is applied to a skin section containing hair ducts, infiltrating at least some of the particles into follicles in the hair ducts, and applying to the skin section electromagnetic radiation having a frequency that is absorbed by the metallic particles. Radiation absorbed by the particles is transferred to surrounding follicular tissue in the form of heat. Depending on the phase of growth, thermal damage to the hair follicles can activate or retard hair growth.

The details of one or more embodiments of the invention are set forth in the accompanying drawings and the description below. Other features, objects, and advantages of the invention will be apparent from the description and drawings, and from the claims.

DESCRIPTION OF DRAWINGS

FIG. 1 is a schematic drawing of a section of human skin showing a cross section of one hair and associated skin structures.

FIG. 2 is a drawing showing a hair passing through the nine stages of the hair growth cycle. SG = sebaceous gland; ORS = outer root sheath; IRS = inner root sheath; DP = papilla.

FIG. 3 shows the morphology of a plucked hair in anagen phase. The full hair matrix is shown as plucked from the end bulb. The lower portions of anagen hairs are soft and

malleable, and may have a tendency to bend over after plucking so that they appear to be curved, or even hooked at their ends.

FIG. 4 shows the morphology of a plucked hair in telogen phase. The club-shaped tip at the bulb end is the distinguishing characteristic of a hair in the telogen phase.

5 FIG. 5 shows the location of five sites (#'s 1-5) on the left hand of a human patient used as test sites to determine a phase shift in the hair growth cycle caused by laser illumination.

FIG. 6 shows the location of two sites (#'s 6-7) on the right hand of a human patient used as test sites to determine a phase shift in the hair growth cycle caused by laser illumination.
10 tion.

FIG. 7 shows a photograph of a hair in anagen phase from site #5 on day 8 post illumination.

FIG. 8 shows a photograph of a hair in telogen phase from site #5.

FIG. 9 is a graph showing the length of hair above the skin surface at site # 4 (-●-), site
15 #5 (-■-), site #6 (-▲-), and site #7 (-▼-).

FIG. 10 is a graph showing the length of hair below the skin surface at control site #5 (-■-), and lased site #4 (-●-).

FIGS. 11A-D are a series of graphs showing the average length of the hair above the skin surface at times zero to 12 weeks after laser treatment without waxing, wherein -●-
20 represents the average length of the unlased hairs (controls) for the four subjects, and -■- represents the average length of the lased hairs for the four subjects.

FIGS. 12A-D are a series of graphs showing the results of measurements to determine the average length of hairs below the skin surface for the four subjects over the period from days 4 to 12 post lasing, wherein -●- represents the average length of the unlased hairs (controls) for
25 the four subjects, and -■- represents the average length of the lased hairs for the four subjects.

FIG. 12A is a graph showing the results on the backs of the subejcts. FIG. 12B is a graph showing the results on the forearms of the subjects. FIG. 12C is a graph showing the results on the thighs of the subjects. FIG. 12D is a graph showing the results on the axilla of the subjects.

FIG. 13 is a graph showing the cross sectional profiles of fluence rates of 3.0, 2.5, 2.0, 1.5, 1.0 and 0.5 J/cm² in the r-z plane for fluence in an incident 7mm square beam of 1 J/cm² using energy per pulse of 0.5 J.

FIG. 14 is a graph showing fluence in skin at depths from zero to 5mm for laser light having the same parameters as in FIG. 13. Fluence is shown on the y axis using an exponential log scale. L_{eff} is shown to be equal to about 1.4mm.

FIG. 15A is a graph showing the broadening of laser beams with fluence of 1 J/cm² of different diameter in skin with depth. -o- at bottom = diameter of 0.2mm; -□- = diameter of 0.5mm; -Δ- = diameter of 1mm; -▲- = diameter of 2mm; -◇- = diameter of 4 mm; -○- at top = diameter of 7 mm.

FIG. 15B is a graph showing fluence levels in the center of laser beams at skin depth for beams of different incident diameters. The incident beam has a fluence of 1 J/cm². The symbols are as in FIG. 15A.

FIG 16A is a drawing showing a mask that receives a large incident laser beam and transmits a plurality of small laser beams for infiltrating contaminant particles into hair ducts.

FIG 16B is a drawing showing an array of lenses that receives a large incident laser beam and transmits a plurality of small laser beams for infiltrating contaminant particles into hair ducts.

FIG. 17 is a drawing showing an occlusive dressing covering a section of skin to which a lotion containing carbon particles has been applied and infiltrated into hair ducts.

FIG. 18A is a schematic drawing showing a hair within a hair follicle.

FIG. 18B is a schematic drawing showing a contaminant lotion applied to the opening of the hair follicle of FIG. 18A.

FIG. 18C is a schematic drawing illustrating that during laser irradiation, some forces are not directed into the follicle. Certain inertial and fluid effects prevent delivery of the contaminant into the bottom of the hair follicle.

FIG. 18D is a schematic drawing showing the embodiment wherein a hydrogel barrier is applied over a contaminant layer.

FIG. 18E is a schematic drawing showing that, upon illumination, the hydrogel layer confines the pressures and shock so that the contaminant is directed into the hair duct around the hair.

FIG. 18F is a schematic drawing showing the contaminant delivered deep into the hair
5 duct surrounding the hair.

FIG. 19A is a schematic drawing of the composite hydrogel showing film 24, layer 26, and coating 30 of an indicator material in an open work pattern.

FIG. 19B is a drawing showing samples of open work patterns for the coating of indicator material in dots 32, intersecting lines 37 and cross-hatched lines 39.

10 FIGS. 20A-C illustrate the hair removal method using large and small particles in the contaminant. →=photomechanical response; ~~~~~=photothermal response.

FIG. 20A schematically represents the transfer of photothermal energy to tissue surrounding a hair duct infiltrated with contaminant carbon particles with diameters in the 1.0 to 50 nanometer range.

15 FIG. 20B schematically represents the transfer of photomechanical energy to tissue surrounding a hair duct infiltrated with contaminant carbon particles with diameters of about 1.0 micron.

FIG. 20C schematically represents the combined transfer of photomechanical and photothermal energy to tissue surrounding a hair duct infiltrated with a combination of the
20 contaminant carbon particles of FIGS 20A and 20B.

FIGS. 21A-E are drawings illustrating various types of microcarrier particles for delivering a sunlight-activated photochemical to hair ducts. FIG. 21A shows a multilamellar liposome; FIG. 21B shows an erythrocyte shadow encapsulating the photochemical; FIG. 21C shows a coacervate droplet containing the photochemical; FIG. 21D shows a latex sphere with
25 monoclonal antibodies attached thereto; and FIG. 21E shows crystal particles with molecules of a photochemical bound thereto.

FIG. 22 is a schematic drawing showing penetration into hair ducts of microcarriers having a photochemical associated therewith.

FIG. 23 is a schematic drawing showing use of ultrasound vibration to enhance
30 penetration of the microcarriers into hair ducts.

FIG. 24 is a drawing showing a computer system connected to a laser.

FIG. 25A shows an uneven skin surface with incident light beam C refracted.

FIG 25B shows the skin surface of FIG 25A covered with an index-matched liquid coating with light beam C penetrating the liquid coating and the skin surface without reflection or refraction.

FIG 25C shows a contact plate placed atop a skin surface covered with an index-matched liquid of FIG. 25B.

FIG. 26 is a cross-section showing a domed reflector covering a section of hair and skin.

FIG. 27 shows a domed reflector with an attached handpiece.

FIG. 28 shows a domed reflector on top of a liquid covering a cross section of skin and hair.

FIG. 29 is a schematic drawing showing a cross-section of a hair duct filled with a light guiding liquid. A photon of light 2 that enters the hair duct is guided to the base of the hair duct by internal reflection and absorbed there in blood vessels in the bottom of the hair duct. Photon 1 incident upon the epidermis is absorbed, while photon 3 is scattered by epidermis.

FIG. 30A is a graph showing the calculated temperature rise at the center and wall of a $5\mu\text{m}$ diameter blood vessel as well as in the surrounding tissue when illuminated by photons at 415 nm wavelength with 0.2 J/cm^2 fluence and pulse duration of $100\mu\text{s}$. Solid line = T at center of blood vessel; dotted line = T at distance one radius away from wall of blood vessel; dashed line = T at distance two radii away from wall of blood vessel.

FIG. 30B is a graph showing the calculated temperature rise at the center and wall of a $5\mu\text{m}$ diameter blood vessel as well as in the surrounding tissue when illuminated by photons at 415 nm wavelength with 0.6 J/cm^2 fluence and pulse duration of 1ms. Solid line = T at center of blood vessel; dotted line = T at distance one radius away from wall of blood vessel; dashed line = T at distance two radii away from wall of blood vessel.

FIG. 31 shows the corresponding increase in skin temperature beneath the skin surface when the skin surface is maintained at 0°C by cooling. Solid line = T increase at $50\mu\text{m}$ beneath the skin; dashed line = T increase at $100\mu\text{m}$ beneath the skin. With pulse

durations longer than 100 μ s, the temperature rise at the interface of the epidermis and dermis, where skin melanosomes are located, is very small so there is little risk of their destruction.

FIG. 32 is a graph showing the temperature increase in tissue surrounding a hair duct caused by laser irradiation, with a = radius of the hair follicle = 25 μ m; and R = the distance of the tissue from the center of the hair follicle. Solid line, $R = a$; dotted line, $R = 2a$; dashed line, $R = 3a$.

FIG. 33 is a graph showing the temperature (T) profile with depth of skin when the skin surface is cooled prior to long pulse laser irradiation according to the method of the invention. Solid line = T at 100 μ m; dashed line = T at 500 μ m; dotted line = T at 250 μ m.

FIG. 34 is a graph showing the temperature (T) profile in skin tissue with depth after the skin surface has been exposed to cooling at 0° C for 2 seconds. Lower solid line = T at 100 μ m; lower dotted line = T at 250 μ m; lower dashed line = T at 500 μ m; line of alternating dots and dashes = T at 1mm; upper solid line = T at 2mm; and upper dotted line = T at 3mm.

FIG. 35 is a schematic drawing showing a laser system including a laser control, an articulated arm for directing a laser beam, and a laser beam in spaced relation to a contaminant on a section of skin.

FIG. 36 is diagrammatic section view of a hair in a section of skin, with metallic particles applied to the skin surface according to a feature of the invention.

FIG. 37 is a view of the hair and skin section of FIG. 36, illustrating the use of magnetic repulsion to encourage the metallic particles to move down the hair duct.

FIG. 38 is another view of the hair and skin section of FIGS. 36 and 37, to which RF radiation is being applied.

Like reference numbers and designations in the various drawings indicate like elements.

DETAILED DESCRIPTION

No. 1: A METHOD OF PRETREATMENT TO SYNCHRONIZE HAIR GROWTH PRIOR TO HAIR REMOVAL PROCEDURES

5 Individual hairs in any given area of skin surface are not normally synchronized at a common point in the hair growth cycle. However, at any time some proportion of hairs in a skin section are in the anagen phase of the hair growth cycle. Hair stem cells and other follicular tissue are believed to be more susceptible to long term damage when they are activated, *i.e.*, in the anagen phase of the hair growth cycle. However, during the mature
10 anagen phase, the hair follicle is fully extended (to a depth of about 3.0 to 5.0 mm), and the distance to the bottom of the follicle from the skin surface is about twice that during the telogen phase of the hair growth cycle. This combination of circumstances makes laser-assisted hair removal difficult, particularly if the method of hair removal depends upon topical application of a substance, such as a contaminant, that is infiltrated throughout hair
15 ducts to aid in the hair removal process.

This problem is overcome in one aspect of the invention by pretreating a skin section to be treated for hair removal so as to synchronize the hairs in the late telogen/early anagen phase. During this transition from the inactive to the active phases of the hair growth cycle, the hair follicle is still weak and shallow (at a depth of from 1.0 to 2.0 mm), yet the hair cells
20 responsible for hair growth are just beginning to be activated and are, therefore, more susceptible to damage than at other phases of the hair growth cycle. FIG. 1 shows a section of human skin with a cross section of a hair shaft 33, a hair duct 31, a nerve ending 34, a sweat gland 35, a sebaceous gland 38, and arteries 36, veins 37 and papilla 32.

This aspect of the invention provides a method for synchronizing the hair cycle of the
25 hairs in a particular area of skin surface. There are nine phases or stages in the hair growth cycle: anagen II, IV, V and VI (growth phases), catagen III, V, VI and VII (regressing phases), and telogen (resting phase) as shown in FIG. 2. During the telogen phase, the follicle shrinks until the bottom of the follicle and the follicle papilla abut the bulge area. This process may be assisted by contraction of the hair root canal cells (similarly to smooth
30 muscles cells) so as to drag the hair papilla to a position nearer the skin surface. Recent work

has shown that stem cells located in the bulge area are responsible for hair regrowth during the anagen phase. At some point during telogen phase, the "normally slow cycle," stem cells of the bulge area are transiently activated, presumably by signals from the abutting follicular papilla. In response, the stem cells, which are responsible for hair regrowth, proliferate, shifting the hair into anagen phase. During the anagen phases, the follicle again extends to its full length, so that the bulge area of the hair duct is located about one-half way down the follicle just below the sebaceous gland. It is known to treat hair for hair removal during the anagen stage when the rapidly proliferating stem cells are easily damaged. However, at anagen stage the stem cells are located at a depth as great as 3.0 to 5.0 mm below the surface of the skin.

In one embodiment, the goal is to prepare a section of skin for hair removal and/or long-term inhibition of hair growth. It has been discovered that once the hairs are synchronized in the telogen/early anagen phase of the growth cycle, hair removal can be accomplished with increased efficiency by any known method. For example, one method includes irradiation of the synchronized follicles with light absorbed either by a naturally occurring chromophore in the hair duct, such as melanin, or by an externally applied light-absorbing contaminant infiltrated into hair follicles.

The hairs on a section of skin are synchronized in the late telogen/early anagen phase by irritating or slightly damaging the hair follicles in a section of skin so as to stimulate hairs in the skin section that are in a catagen or telogen phase to shift into anagen phase of the hair growth cycle. The irritation can be provided by mechanical, thermal, or chemical means. Any of these means will increase the flow of blood to the hair follicles. The only requirement is that the irritation or damage be sufficient to activate the natural repair response to slight damage or injury, but not sufficient to cause severe damage such as would cause hairs already in the anagen phase to be shifted to an inactive state.

For example, synchronous growth of human hair can be effected by application of a drug, such as Minoxidil, which increases flow of blood to the hair follicles, or application of Methionine (for example post waxing) to increase proliferation of papilla or matrix cells. Such drugs can be introduced into the hair root canal either by direct application or delivery in microcapsules.

Alternatively, mild laser treatment of a skin section containing resting hair cells, or irradiation by a flash lamp, can be used to shock anagen phase hairs into telogen phase while stimulating the resting cells to transition into the anagen phase, thus synchronizing the hair cells in the growth cycle. In addition, waxing, plucking, or electrolysis of hair follicles can be used to provide the shock necessary to synchronize hair growth. The degree of irritation or mild injury administered is that sufficient to trigger the natural self-protective repair mechanism that shifts hairs to the telogen/early anagen phase without causing severe damage to the hair cells in the bulge area of the hair follicle. FIG. 35 shows a laser system 74 useful for illuminating a skin surface including a laser 76, a laser control 78, an articulated arm 80 for delivering a laser beam, and pulses of laser light 82 in spaced relation to a section of skin 12 having a contaminant 14 thereon.

Following application of the shock or irritant, a period of time is required for the phase shift to occur, for example a period of from about 3 to 25 days. It has been discovered by empirical tests that good results can generally be obtained by waiting for a period of about 7 to 21 days following administration of a shock or irritant for the hairs in a section of skin to substantially synchronize. Therefore, if the treatment to synchronize the hairs to telogen/early anagen phase growth is preparatory to administering a subsequent hair removal treatment, a period of about 7 to about 21 days should generally be allowed for the phase shift to occur before the subsequent hair removal treatment is undertaken.

Once hair growth is synchronized in late telogen/early anagen phase, the skin surface can be illuminated with short pulses of light at a frequency absorbed by a naturally occurring chromophore or externally infiltrated contaminant. For example, a ruby laser can be used to irradiate the melanin within shortened hair follicles. Methods of hair removal that depend for their effect upon the ability to infiltrate a light-absorbing contaminant deep into the hair follicle, such as those disclosed in U.S. Patent Nos. 5,226,907 and 5,425,728, are enhanced by use of the invention. During the mature anagen period of the hair growth cycle when it is easiest to damage stem cells and other follicular tissue involved in hair growth, it is hardest to infiltrate the contaminant to the bottom of the hair follicle, and thereby ensure destruction of follicular tissue throughout the length of the hair duct. Synchronizing hair growth in the late

telogen/early anagen phase greatly reduces the distance into a hair duct that a contaminant needs to be infiltrated.

When the hair removal treatment to be employed on the synchronized hairs utilizes an external contaminant infiltrated into the hair ducts, the pretreatment method can incorporate the following steps. First, a contaminant, *i.e.*, one containing light absorbing chromophore particles, is gently applied to the skin section so that at least a portion of the contaminant enters the upper region of the hair follicles. For instance an oil or water-based suspension of carbon particles or other chromophore particles that absorb light in the near IR region of the spectrum, can be employed as the externally applied contaminant. Liposomes can also be used to deliver into the hair follicles any chromophore which has a good absorption at a laser wavelength that is appropriate for illumination of a skin section. Hair papilla and/or matrix cells can also be stained with a dye which has good absorption of light, using coherent or non-coherent light radiation. A mild concentration of a photosensitizer chemical (*e.g.*, one that is activated by laser radiation to produce singlet oxygen) can also be administered to a skin section, allowed to become absorbed in hair growth cells, and then used to shock the hair follicles. Alternatively, a mild solution of a chemical that causes irritation to hair follicles upon contact can be administered to synchronously stimulate hair growth. For example levulenic acid applied to the skin surface so as to infiltrate into hair ducts in a concentration of about 0.002 to about 2 percent by volume will cause a mild irritation that will shock hair follicles.

The skin section can be cleaned using a non-irritating cleaner prior to application of the contaminant to remove oil and debris, such as lint and loose skin cells. For example, lint and cell debris can be removed from the skin section with any type of tape having a light adhesive, such as is used for lint removal from fabrics, and the like. Another example of a non-irritating cleaner is isopropyl alcohol. The skin section generally should not be vigorously brushed or rubbed during cleaning prior to administration of the contaminant because irritation will cause sebaceous glands in the hair ducts to exude a liquid wax that will obstruct entry of a contaminant.

As one example, the contaminant can be a suspension of carbon particles in the size range from about 0.2 to about 0.01 micron (carbon black) or in the size range up to about 1

micron. The carbon particles are suspended in or mixed with a light oil, such as light mineral oil, NF. Drakeol 13™ (PennDrake, Los Angeles, CA), is a preferred oil for this use.

When applied to the skin section prior to irradiation, at least a portion of the contaminant must enter the upper region of the hair follicles, *i.e.*, the mouth of the hair follicles.

5 Generally, merely applying the contaminant to the skin surface will cause the particles to infiltrate only about 20 microns into the hair follicles. Increased penetration of a contaminant containing oil may be obtained by allowing the contaminant to rest on the skin section for a period of time sufficient for the opening of the hair follicle to become enlarged before the next step is taken. This effect is thought to be due to the action of the light oil on the skin and
10 hair follicles. Usually, allowing an oil-based contaminant to remain on a skin section for a period of about 15 minutes is sufficient to enlarge the openings of hair follicles to the fullest extent.

Next, to shock the hair follicles, the contaminated skin section is illuminated with one or two short pulses of light having a frequency highly absorbed by the contaminant particles.
15 For example, if the contaminant contains carbon particles, a frequency is used that is well absorbed in carbon, but relatively transparent to skin, such as is provided by a Nd:YAG laser. Additional useful light sources are discussed in the Tankovich patents incorporated herein by reference.

In one embodiment of the invention, it is desirable to explode or fracture the contaminant particles in the hair ducts during illumination to drive them as far as possible into the
20 depth of the hair follicles. In any event, it is necessary to irritate or mildly damage the follicular tissue, but only enough to trigger a natural repair mechanism in the follicles, causing any follicles in anagen phase to pass out of anagen phase into telogen phase. Short pulses of light having a low fluence in the range from about 1 to about 2.5 J/cm² can be used
25 to avoid transferring substantial heat and/or kinetic energy from the chromophore particles to the hair follicles or surrounding tissue. Serious damage to the hair papilla should be avoided. Therefore, preferably no more energy is administered to the hair follicles during the pretreatment process than will raise the temperature of the follicle walls more than about 10° C to about 20° C above body temperature during the laser pulse.

During the rest period of about 7 to 21 days following administration of the shock, hair cells in anagen phase will cycle through telogen phase into early anagen phase, a point in the hair growth cycle referred to herein as "late telogen/early anagen phase." However, if too much heat is transferred to the hair follicles during the pretreatment, hair growth generally will not be synchronized.

After observing the rest period to allow synchronization of hair growth in the "late telogen/early anagen phase," a hair removal procedure can, in many cases, be undertaken with the expectation of an increased level of success. It has been discovered that when the hair growth cycle has been synchronized using the method of this invention, the percentage of hairs that are sufficiently devitalized to inhibit regrowth for an extended period of time (for example 3 to 6 weeks, or longer) is substantially increased.

Use of a contaminant for shocking the papillae is optional, and is omitted if the light absorbing chromophore to be illuminated during a hair removal procedure is naturally occurring, such as melanin in the hair ducts.

Sample process parameters useful when the pulses of light used in the skin pretreatment process of this invention are provided by a Nd:YAG laser and the contaminant comprises light mineral oil and carbon particles are as follows:

Wavelength	about 1064 nm
Beam Shape:	circle or square
Beam Size:	about 8 mm diameter (circular) or 7x7 mm (square)
Fluence	1-2 J/cm ²
Pulse energy	0.5 J/pulse

In some cases it may be advantageous to repeat the pretreatment process from 1 to about 3 times before a procedure is attempted to illuminate the hairs with sufficient energy to cause hair removal and/or long term inhibition of hair growth. Alternatively, for particularly resistant sites, the pretreatment of this invention can be alternated with the laser hair removal treatment in fairly rapid succession. For instance, success has been obtained in the long-term inhibition of growth of a man's beard by three repetitions of the pretreatment/treatment cycle, spaced apart by a rest period of about 3 to about 5 days. The illumination at pretreatment was

at 1.5 J/cm² to infiltrate the contaminant, and drive the follicles into telogen phase. The illumination for hair removal following the rest period was at 3.0 J/cm². In this embodiment of the invention, due to the short rest period, the contaminant introduced during each of the pretreatment procedures remained in place and was not replenished before the subsequent hair removal treatment, which followed immediately after the rest period was completed.

In yet another embodiment of the invention, the pretreatment method comprises the following steps. An oil-based contaminant containing a light-absorbing chromophore is applied as described above to the surface of a section of skin. The contaminant may be allowed to rest upon the skin for a period of time sufficient for the opening of the hair follicle to become enlarged, for example, about 15 minutes, before the next step is taken.

Next, a hair removal wax is applied over the oil-based contaminant on the skin surface and is allowed to dry. Any commercially available wax intended for hair removal can be used, for example Azulene™ or Ember™, both hard waxes, or Epillyss™, a soft wax. To adhere the wax to the skin surface, application of the wax commences from a location on the skin surface just outside the area covered with the oil-based contaminant. Adjacent strips of wax should overlap to form a covering that completely bridges the oily area and adheres to oil-free skin surface around the periphery. Once the wax has been allowed to thoroughly dry according to the manufacturer's instructions, the wax is stripped from the skin. Surprisingly, in the waxed area a significant proportion of the hairs will be removed from the hair follicles even though the wax was applied to water or oil-coated hairs. In addition, stripping the wax and extracting hairs from the hair follicles causes the light-absorbing particles to infiltrate throughout the hair follicles more completely. The stripping action also subjects the hair follicles to sufficient shock to synchronize hair growth after a rest period is observed, as described above. Following the rest period, hair removal procedures can be undertaken with the expectation of an increased level of efficiency.

This aspect of the invention having been fully described, it is further illustrated by the examples below. It will be understood, however, that the invention is not limited by the examples but is defined by the appended claims.

Example 1

The following set of experiments was conducted to determine the period of time required after administration thereto of an irritant or shock for hair follicles to enter the late telogen/early anagen stage of the hair growth cycle. The data obtained indicates how long the rest period should be between administration of the shock and commencement of a hair removal procedure.

The lower left forearm, wrist area, and hand of a human patient was selected as the location of the test sites. The untreated right hand and arm of the subject was used as a control. The locations on the subject's left hand and arm selected as test sites had been lased 2 months before this treatment, but 100% of the hairs had grown back. In addition, reference photographs of hairs in anagen and telogen phase were used for comparison with hairs plucked from the test sites. FIG. 3 shows the morphology of a plucked hair in anagen phase, with the full hair matrix shown as plucked from the end bulb. The lower portions of anagen hairs are soft and malleable, and may have a tendency to bend over after plucking so that they appear to be curved, or even hooked at their ends. FIG. 4 shows the morphology of a plucked hair in telogen phase. The club-shaped tip at the bulb end is the distinguishing characteristic of the telogen phase hair.

The test sites on the left hand, as shown in FIG. 5, were as follows:

<u>site #</u>	<u>Treatment protocol</u>
1	Pluck hair, lase continuously with multiple passes 5 days after plucking
2	Pluck hair, lase continuously with multiple passes immediately after plucking
3	Pluck hair, no lasing
4	No plucking; lase continuously with multiple passes immediately after plucking, close shave hair after lasing
5	Close shave hair, no lasing

On the right hand, as shown in FIG. 6, the treated sites were as follows:

<u>site #</u>	<u>Treatment protocol</u>
6	Close shave hair, no plucking
7	Close shave hair, no plucking

5

For lasing, a Nd:YAG laser operating with a wavelength of 1.06 microns, repetition rate of 10 Hz, fluence of 3.0 J/cm² was used.

Eventually, all hairs above the skin surface in the test areas were plucked (#1-3) or shaved (#4-7). Sites # 5, 6, and 7 are controls for site #4, and site #3 is a control for sites #1 and 2. Records of hair regrowth were kept for all sites. The time for regrowth to reach a length of 3mm was recorded. The hair was shaved as 3mm of regrowth was exceeded. Records of hair density were also kept. Density was estimated by eye, by comparison with shaved and unshaved control areas on the right hand, which showed density and appearance at the beginning of the study. One-fourth of the hairs from each test site were plucked at each of weeks 1, 2, 4, and 6 post lasing for examination by microscope to determine the effect of laser induced modifications.

15

On day 8, hairs from site #7 were plucked for measuring. By comparison with the reference photograph of FIG. 3, the hair bulbs showed that the hairs were in anagen phase. By contrast, on day 8, hairs from site #4 were completely bleached and showed a tapering tip in the place of the hair bulb. The results of the tests at day 8 are shown in Table 1 below.

20

Table 1

Site #	# of hairs	anagen	telo-gen	tapering	broken	mean length (mm)
4	48	0	3 (6%)	45 (94%)	0	2.79±0.25
7	27	24 (89%)	2 (7%)		1	4.4±0.4

25

FIG. 7 shows a photograph of a hair from site #5 on day 8. The lower portion (the bulb) is pigmented (dark brown) and the shape is straight, indicating that the hair is in anagen phase. By comparison, another hair from site #5 shown in FIG. 8 is transparent, indicating a

lack of pigment (lack of melanin) and the bulb has a club shape. These characteristics indicate the hair is in telogen phase.

On day 14, hairs from site #4 would slide easily out of the follicle when pulled. The tip of the shaft was normally pigmented (pigmentation had recovered as compared to the rest of the shaft), but the tip was about 50% smaller than the rest of the shaft. Of the 18 hairs plucked from each site on day 14, the average length of the whole plucked hair was as follows:

Site #4 2.5 ± 0.4 mm

Site #7 5.4 ± 0.6 mm

On day 18, follow-up studies of hairs from sites #4 and #7 were conducted by microscopic examination and measurement of plucked hair shafts, with the results shown in Table 2 below:

Table 2

Site #	# of hairs	ana-gen	telo-gen	taper-ing	broken	mean length (mm)
4	13	0	1	12	0	7.1 ± 0.3
7	17	15	1	1	0	2.5 ± 0.35

The hairs from sites # 4-7 were also measured to determine the length of the hairs above the skin and the length of the hairs below the skin. The results of these studies are shown in FIGS. 9 and 10. The length of the hairs above the surface from lased site #4 clearly showed inhibition of hair growth as compared with the length of hairs from control sites. From these studies it was determined that 18 days after lasing, the hair bulbs for hairs in site #4 were less than 1 mm below the surface of the skin, while the hair bulbs of hairs from the control site were at a depth of about 2.5mm beneath the surface of the skin. Thus, the hair ducts of the treated site had contracted as a result of being shocked. This data confirms that the lasing was sufficient to cause hairs at site #4 to pass into telogen phase.

Discussion of results

On the laser treated sites, hair kept growing above the skin surface at the same rate as on the untreated (control) site during the first 4-8 days after treatment. Growth of hairs on the laser treated sites slowed down, then stopped, and the hairs fell out within the next 1-2 weeks. By contrast, the hairs on the control site continued to grow, obtaining a length that increased linearly with time.

Anagen and transition stage hairs on the laser treated site showed significant morphological changes (tapering at the hair bulb end) as early as the 4th day after treatment. This phenomenon continued until the hairs fell out. By contrast, telogen hairs remained unaffected by laser treatment and continued to follow a normal growth cycle.

When hairs that showed modifications after laser treatment were plucked, they were found to be half as long below the skin surface as were the normal untreated hairs (controls). Hairs that were not plucked showed bleaching down to the root, and then 1-2 weeks later started to recover pigmentation at the tapering end. Slim pigmented "tails" could be seen at the recovering end, yet the hairs never returned to normalcy and never resumed a normal growth cycle.

About three weeks after lasing, hairs started growing back in significantly reduced number in the laser-treated site. About 20% regrowth was observed 38 days after laser treatment. No telogen hairs were found on the laser treated sites 38 days post lasing, suggesting that telogen hairs were unaffected by laser treatment and synchronously cycled into active growing anagen hairs.

Black material in the upper portion of the hair follicles under the stratum corneum became visible on the laser treated sites about 2 weeks after treatment and remained visible without any signs of hair growth in the follicles. The dots of black material did not disappear after extensive lasing at 1.06 microns wavelength and 3.0 J/cm² fluence.

Example 2

The procedures of Example 1 were repeated using four human subjects, except that four different sites were used for each subject: back, forearm, thigh and axilla. Control, unlased sites were also utilized at each of the four locations for each subject. FIG. 11 is a

graph showing the average length of the hair above the skin surface at times zero to 12 weeks after laser treatment without waxing, wherein -●- represents the average length of the unlased hairs (controls) for the four subjects, and -■- represents the average length of the lased hairs for the four subjects. The inhibition of hair growth caused by the mild laser treatment to shock the hairs was greatest on the back, thigh and axilla. Growth of hairs on the forearm was least affected.

FIG. 14 is a graph showing the results of measurements over the period from days 4 to 12 post lasing to determine the average length of hairs below the skin surface for the four subjects wherein -●- represents the average length of the unlased hairs (controls) for the four subjects, and -■- represents the average length of the lased hairs for the four subjects. These results show that the shortening of the hair duct (as occurs during telogen phase) had begun as early as four days post lasing.

Example 3

Monte Carlo simulation studies were conducted using known methods to calculate the actual fluence profile in human skin or flesh when the skin surface is illuminated with a Nd:YAG laser having a wavelength of 1.06 microns, with fluence in the incident beam of 1 J/cm², and energy per pulse of 0.5 J.

Optical and geometrical properties at the wavelength value of 1.06 μ m are summarized in Table 3 below:

Table 3
Optical Properties for skin model

	μ_s	μ_a	g	n	depth (mm)
Epidermis	2	300	0.85	1.4	0.065
Dermis	1	100	0.85	1.4	Infinite

The effective penetration depth (L_{eff}) of light into tissue is estimated in general light diffusion theory as follows:

$$L_{eff} = [3\mu_a\mu_s(1-g)]^{-1/2}$$

Utilizing the data from the Table 3, the calculated penetration depth (L_{eff}) in dermis is about 1.5 mm.

In the model, a collimated laser beam is incident on the skin at a right angle to its surface. The skin model consists of two domains, which imitate the properties of the epidermis and dermis. The epidermis is considered as an infinite slab 65 μm wide. The dermis is considered as a semi-infinite domain having a common plain interface with the epidermis and extending infinitely along the interface.

Simulation Method

Propagation of light in skin was simulated by the Monte-Carlo (M-C) method, in which absorption and scattering phenomena in highly light scattering media has been properly accounted, as well as refraction and reflection of light at the interfaces. Software utilizing known mathematical formulae was used to make the calculations.

In simulation, the tissue was divided into a 3D array of small (0.2 mm on a side) cubic volume elements, the amount of light energy absorbed inside each element was estimated, and the local energy fluence rates were retrieved to enable a 3D representation of the radiation level within the tissue. In this way, fluence rates in both vertical (radius-depth or r-z) and horizontal (x-y) cross-sections were estimated and displayed in contour plots. In all simulations, the origin was on the skin surface in the center of symmetry of the incident beam. Depth was measured from the epidermis-air interface into the tissue.

For economy of time, the simulation procedure was divided into two stages. The first stage included M-C simulation of fluences in a selected cross section with a 0.2 x 0.2 mm² (pixel) incident beam and a fluence rate in the beam of 1 J/cm². At the second stage, a desirable beam shape was approximated with square beam pixels, and then fluences were added up to calculate ultimate fluence rate for each particular beam profile and cross section.

For different skin models or reflector conditions, a new M-C simulation with pixel beams was performed. Results of simulations obtained by the two stage method has been shown to be identical to those generated with conventional M-C, other conditions being equal.

Cross sectional profiles of fluence rates in the r-z plane of 3.0, 2.5, 2.0, 1.5, 1.0 and 0.5 J/cm² were plotted for fluence in the incident beam of 1 J/cm² using a 7mm diameter round beam with energy per pulse of 0.5 J. A plot of these fluence profiles is shown in FIG. 13.

FIG.14 shows a plot of fluence in skin at depths from zero to 5mm for laser light having the same parameters as in FIG. 13. Fluence is shown on the y axis using an exponential log scale. L_{eff} is shown to be equal to about of 1.4mm.

The methods of this invention provide several advantages. When the papilla is in a position proximate the skin surface, it is more easily reached by light energy administered to the skin surface, and thus is more susceptible to damage at low fluence, *i.e.*, in the range from about 3-5 J/cm². Because stem cells are more susceptible to long term damage when they are activated, increasing the percentage of the hairs in late telogen/early anagen phase increases the number of hairs in any given section of skin that are sufficiently damaged by such techniques to effect long term inhibition of hair growth. Thus, by utilizing the pretreatment method of this invention, the energy required to effect permanent hair removal is minimized because the distance below the surface of the skin to which light energy must penetrate during a hair removal treatment is minimized, and the percentage of hairs for which the future growth is significantly inhibited can be increased. Both goals are attained while minimizing undesirable damage (burning) of surrounding tissue.

No. 2: METHODS AND DEVICES FOR INFILTRATING CONTAMINANT IN LASER-ASSISTED HAIR REMOVAL

Many hair removal procedures involve application of a contaminant containing light-absorbing particles to the surface of a section of skin for the purpose of inhibiting the growth cycle of hairs in the skin section, or for long term inhibition of hair growth in a skin section. The skin section and hair ducts therein containing the contaminant are illuminated by a beam of light at a wavelength absorbed by the contaminant for the purpose of (1) driving particles in the contaminant into the lower region of hair ducts (propulsion phase) and (2) causing the particles to heat up (thermal phase). Heat is thereby delivered preferentially to hair growth cells at the base of the hair ducts. However, it is difficult to produce a net downwards vector

on a particle sufficient to drive it into the depths of the hair duct because light incident upon a skin surface is randomly scattered and absorbed during passage through the epidermis and dermis of the skin. In addition, sebaceous glands in hair ducts tend to exude a sticky wax-like substance that impedes movement of chromophore particles into the base of the hair ducts.

5 In addition, the skin structures that are targets of various laser treatments are found at different depths in skin. It is known to vary the wavelength of the laser beam to control the depth to which a laser beam penetrates into skin so as to direct laser energy only so deeply into skin as is necessary to affect the skin structure that is the target of a laser-assisted skin treatment. Further methods of controlling the depth of penetration of a laser beam into skin
10 would be advantageous.

One aspect of the invention solves this problem by providing an improved method for infiltrating light-absorbing chromophore particles into hair ducts using laser illumination. In one aspect of the invention, a mask is interposed between the light source and the skin section to be treated, and receives an incident large laser beam, but transmits a plurality of
15 small laser beams spaced so as to prevent merging of the beams in the skin surface. These small beams are used to create an energy profile with depth in skin that is useful for creating a net downward force on illuminated chromophore particles in hair ducts to drive the particles into the depths of the hair ducts. In another aspect of the invention, an array of lenses is substituted for the mask to transform an incident large laser beam into a plurality of
20 small beams spaced so as to prevent merger of the small beams.

A beam of light incident upon a skin surface is progressively attenuated with increasing depth due to absorption and scattering of photons. The gradient in skin of energy attenuation depends upon the beam size. The gradient of energy attenuation is relatively flat if the beam of light is relatively large (*i.e.* 7 to 8 mm in diameter). Photons that penetrate skin
25 without absorption (*i.e.*, such as those provided by a Nd:YAG laser) tend to be randomly scattered during passage. Due to the random scattering effect, photons tend to strike a particle of contaminant in a hair duct or other skin structures from all directions. In the case of a relatively large beam, a particle is bombarded with photons of comparable energy on all sides, making it difficult to create a net downward vector on an illuminated particle of
30 contaminant, even if some parts of the particle are exploded by the light energy.

It has now been discovered that a small beam of light having a spot size in the range from about 0.5 to 1.0 mm in diameter is attenuated more rapidly with depth than one of larger diameter (e.g., 8 mm in diameter). Thus, the size of the light beam controls the depth at which follicles and other skin structures are affected by a light beam. For more shallow effect, the beam spot size is decreased. As shown in FIG. 15B, the gradient of energy attenuation in skin is correspondingly steeper for small beams, with the steepness of the energy gradient progressively increasing as the beam spot size decreases. Therefore, either a single small beam producing a spot size in the range from about 0.5 to 1.0 mm in diameter or a plurality of small beams of light of such size establish in skin a steep light energy gradient having rapid attenuation with depth.

It has also been discovered that small beams of light in this size range spread out with depth more rapidly than larger beams (FIG. 15A). Therefore, if a plurality of small beams are used simultaneously to create a steep energy gradient within skin, the small beams must be spaced apart a sufficient distance to prevent the small beams from merging beneath the skin surface and taking on the characteristics of a large composite beam. Accordingly, the plurality of small beams are usually spaced at a distance that approximates the effect of an infinite distance, for example about 0.5 to 1.0 mm between the circumference of the beam spots.

Due to the large energy gradient of attenuation established by a single small beam (or by a plurality of small beams of light having the above-described spot diameter and spacing), a photon from such a small beam imparts greater heat energy to the top region of a chromophore particle in a hair duct than a photon from the same beam that strikes the particle at a lower region. The difference in energy between photons striking the top and bottom of a particle infiltrated into skin or into a hair duct is larger, the larger the size of the particle. A photon may strike the top region of a 1 micron particle with sufficient energy to cause a small explosion, but a photon from the same small beam of light, or a photon scattered from a nearby beam of light, that strikes the bottom of the same particle may have lost sufficient additional energy in traveling through skin an extra micron in depth to be incapable of causing an explosion at the point of impact. When this effect is multiplied by a plurality of photons striking each of the chromophore particles in a hair duct, a net downward force is

exerted on the particles. This net downward force is useful for driving the contaminant particle into the depth of the hair duct during laser-assisted hair removal procedures.

In view of these considerations, in one aspect of the invention a single small beam of light is rapidly scanned over the section of skin to be treated. For example a single beam
5 having a spot diameter of 0.5 to 1 mm in diameter with a fluence of about 2.5J/cm², with pulse energy of about 20mJ per pulse, a pulse repetition of about 600 pulses per second, and a minimum pulse duration of about 10 ns could be used to exert sufficient force on graphite particles in hair ducts to drive a portion of the particles into the base of hair ducts. Once the particles are spread into the base of the hair ducts, the laser parameters can be adjusted to
10 those recognized in the art as suitable for heating up the particles so as to transfer heat to tissue surrounding the hair ducts. When a single small beam is used during the propulsion phase, a different laser to provide a beam diameter of about 7 to 8 mm is generally used during the heating phase of the hair removal process.

Alternatively, to avoid having to switch lasers between the propulsion phase and the
15 heating phase, a device can be interposed between the light source and the skin section to be treated that will transform a single large beam (*e.g.*, one of 7 to 8 mm in diameter or a 7 mm square beam) into a plurality of small beams having the size and spacing disclosed herein. One such device is a light-blocking mask having an opaque body with many light-transmissive, small cylindrical apertures, each with a diameter of from about 0.5 to 1.0 mm, with a
20 distance of about 0.5 to 1.0 mm between the circumferences of the cylinders. For convenience, the mask can be adapted for attachment directly to the distal end of a laser wand.

The body of the masque is opaque and can be in any convenient overall size and shape, such as a round or square thin plate, so long as it has one surface that is adapted for contacting a skin surface. Generally the body of the mask is at least 10 times less in thickness
25 as in overall size to prevent the sides of the cylindrical apertures from shading the skin surface as the light passes through the apertures. The apertures in the body are generally oriented perpendicularly to the contact surface of the mask. For convenience in use, the contact surface of the mask generally has an area of about 0.5 to several centimeters square and is generally smooth enough to pass over the skin surface without abrading it. The contact

surface of the mask may be planar or may conform to the shape of a body part, and may be rigid or somewhat flexible.

The mask body can be made of any opaque material that will not be destroyed by laser irradiation having the energy characteristics with which the mask is to be used.

5 Generally, the mask body is heat resistant and will not undergo a chemical reaction caused by the laser. The mask body should produce a minimum of specular reflection to avoid an undesirable effect on the laser, such as might be created if light is reflected back into the laser cavity. For example the surface receiving incident light can be roughened to reflect light in all directions. In one embodiment, the body of the mask is formed of a sheet of fluorescent
10 paper (such as is used for aligning optics containing *infra* red radiation) with pinholes as apertures.

FIG. 16A is a drawing showing a mask 2 with a body 4 having contact area 6 and pinhole apertures 8. Incident light beam 8 is transformed by the mask into a plurality of smaller light beams 9. Attached to the mask is heat sink system 5.

15 In use, light from a light source, such as a laser, passes through the apertures in the mask and is directed to a skin surface and hair follicles through the small apertures in the mask, which have a diameter in the range from about 0.5mm to 1 mm and are spaced apart at a distance of about 0.5mm to 1mm as measured between the edges of the apertures. The size of the apertures and their spacing or density in the body of the mask are selected to create
20 from the large light beam a plurality of small beams. For example, a mask for use with a Nd:YAG laser having a wavelength of about 1064 nm and a beam size of about 8 mm contains round apertures with an internal diameter of about 0.4 to about 0.8 mm and an average spacing between edges of the apertures of about 0.5 to 1.0mm.

Since the mask screens out a substantial portion of the light energy produced by the
25 light source, several passes of the masked light source over a section of skin are required to deliver the same amount of light as does an unmasked light source. A simple calculation can be used to determine the number of passes of light delivered through a mask having apertures of any given diameter and density are required to approximate the energy delivery of a single pulse of unmasked light. The following sample calculation shows the light delivery of a mask
30 having apertures with a diameter of 0.6mm and a density of 60 apertures/cm² :

Diameter of a hair follicle = 0.1 mm;

Diameter of mask aperture = approximately 0.6mm

Effective area S covered by a single aperture = $3.14 (\text{aperture dia.} + \text{follicle dia.})^2$

Area covered by a mask with 60 apertures/cm² after 5 passes = $5 \times 60 \times S = 1.15 \text{ cm}^2$

5

By this calculation, 5 passes of a laser beam of 8mm in diameter delivered through a mask having an aperture density of 60 apertures/cm² delivers to a single hair duct approximately the same energy as one unmasked pulse.

Therefore, several pulses delivered through the mask are required to delivery laser
10 energy equivalent to 1 to 2 pulses of unmasked light. Generally, about 5 or 6 pulses are delivered to each section of skin treated, with the mask being shifted slightly at random between the pulses to even out the amount of illumination. In general, whatever the diameter and density of the apertures in the mask, the number of lasing passes with the mask in place is selected to deliver roughly the same amount of energy per hair duct or other target skin
15 structure as would be received from unmasked light.

In one embodiment, the body of the mask is adapted to absorb heat from the surface of the skin during its illumination. The body of the mask can absorb some quantity of heat from the skin surface, depending upon the heat capacity of the material from which it is made. The capacity of the mask body to absorb heat can be enhanced by having one or more
20 passageways or conduits there through in which a cooling medium is circulated to absorb heat from the skin surface. For example, at least one conduit for the cooling medium can be located around the periphery of the body of the mask in a portion of the body that does not contain the apertures. In addition, as shown in FIG. 15, any known type of heat sink system 5 can be attached to body 4 of the mask, including those provided by thermoelectric cooling,
25 passive heat sinks, convection cooling, such as provided by fans, conduction cooling, prechilling, and the like.

When used as described herein, the mask provides the advantage of increasing the net downward force vector on light-absorbing particles in the hair ducts caused by light photons delivered through apertures in the mask. The mask also decreases the depth of penetration

through skin of an incident light beam and therefore, is useful in any skin treatment in which a shallow penetration of light is required.

In another aspect of the invention, an array of lenses (FIG 16B) is substituted for the mask to transform an incident large laser beam into a plurality of small beams having the above described spot size and spaced at an interval to prevent merger of the small beams. The array includes a plurality of lenses, each having a focal length of about 5mm to about 50mm and a diameter of about 5mm to about 50mm. Although the array can have any overall shape, in one embodiment the lenses in the array are disposed to receive an 8mm diameter incident beam and transform it into a plurality of beams having a spot size of about 0.5mm to about 1.0mm. As shown in FIG 16B the array 84 is arranged circularly, with each lens 86 being semispherical in shape. The array can be either flat or curved. In use, the lenses can be disposed in either direction relative to a skin surface.

The mask or the array is adapted for attachment to a laser wand or laser arm for delivering the small beams to the skin surface during treatment by laser irradiation. Although these devices are described with reference to the advantages of creating a steep energy gradient within skin to facilitate creation of a net downward vector on particles infiltrated at some depth within skin structures, such devices can also be used to create a plurality of small beams to facilitate shallow illumination of a skin surface for any purpose, such as might be useful in a method of laser skin peeling or to affect sebaceous glands.

No. 3: A METHOD FOR INFILTRATING A CONTAMINANT INTO HAIR FOLLICLES USING AN OCCLUSIVE DRESSING

Hair removal procedures are known in which a contaminant is applied to the skin surface and caused to infiltrate into hair ducts for subsequent irradiation by a light source. To effect hair removal, the light absorbing contaminant (usually containing light-absorbing particles) must be driven to a depth in the hair duct that will allow transfer of heat and mechanical energy from the particles directly to tissue surrounding the hair duct that effects hair growth, *i.e.*, the stem cells located in the bulge area and the dermal papilla of the hair duct. Generally, however, massage of the contaminant onto the skin surface causes the contaminant to infiltrate the hair ducts only for about 20 microns, yet the portion of the hair

duct that contains the stem cells and/or dermal papillae is located at a depth of from about 2 to 6 mm. depending upon the location on the body where inhibition of hair growth is desired, *i.e.*, the beard, leg, or upper lip.

5 The present method provides a procedure by which a contaminant, once applied to a skin surface so as to introduce the contaminant into the top region of the hair follicle, can be induced to infiltrate more deeply into the hair follicles to be treated. In the present invention, after application of the contaminant to the skin surface, but prior to illumination, the pores and infiltrated hair ducts in the skin section are occluded for a period of time ranging from several minutes to several hours, whereby further infiltration of the contaminant into the hair
10 ducts is caused.

The invention is described with reference to FIG. 17, which shows occlusive dressing 10 covering a section of skin 12 to which a contaminant 14 containing particles has been applied and infiltrated into hair ducts 31. It has been discovered that when an occlusive covering is applied to a contaminated skin section for an extended period of time, contami-
15 nant in the upper region of the hair ducts is drawn into the lower portion of the hair ducts as shown in FIG. 18. Therefore, occluding the contaminated hair ducts with a covering facilitates loading of particles in the contaminant into the lower regions of the hair ducts. This discovery provides an alternative method for spreading a contaminant, such as one containing light absorbing particles, deep into the hair follicles prior to illumination so that, during
20 illumination of the skin section, the heated particles will transfer energy to the portion of the hair cells surrounding the lower region of the hair follicle that are responsible for hair growth, particularly those in the bulge area.

Any air and water-tight covering can be used as an occlusive dressing. For instance, any type of known liquid that can be painted or sprayed onto the skin to form an occlusive
25 covering can be used. In addition, an occlusive bandage or dressing that provides an adhesive seal at the skin surface around the perimeter of the covered area can also be used. For example, the occlusive dressing sold under the trade name Tegaderm™ bandage can be used to occlude the contaminated skin section.

Allowing the occlusive covering to remain on the contaminated skin surface for an
30 extended period of time is sufficient to induce infiltration of the contaminant into the lower

regions of the hair follicles. The period of time required will vary, depending upon the depth of the hair follicles to be treated. Once this goal has been accomplished, the occlusive covering can be removed from the skin surface, and the skin surface is ready to be illuminated to cause injury to or destruction of the cells surrounding the hair ducts that promote hair growth.

Generally, the covering is allowed to stay in place for a period of time ranging from several minutes to several hours, for example about 15 minutes, whereby infiltration of the contaminant into the lower regions of the hair follicles is induced. Infiltration is optionally further enhanced by application of a surface-wetting agent to the skin surface. A surface wetting agent will facilitate wicking of the contaminant, including any chromophore particles contained therein, into the hair ducts while the pores and hair ducts in the skin surface are occluded, *i.e.*, while sealed with a water-barrier forming substance, or covered with an impermeable patch or bandage. The surface wetting agent can be added to the contaminant, or contained within or upon the occlusive dressing. All that is required is that the surface-wetting agent is present at the mouth of the occluded follicles during the period of time that the occlusive covering is in place.

After removal of the occlusive covering, the skin surface can be illuminated to shock or cause injury or destruction of the cells surrounding the hair ducts that promote the growth of hairs. Any of the methods of illumination that utilize a light absorbing contaminant in conjunction with a light source, such as a laser with a wavelength of light highly absorbed by the contaminant can be employed during the illumination phase. Examples of such methods and procedures, and of the most useful types of contaminants and lasers, are described in full in U.S. Patent Nos. 5,226,907 and 5,425,728, which are incorporated herein by reference, each in its entirety.

For example, laser illumination to inhibit hair growth can be accomplished by infiltrating a contaminant containing carbon particles in the size range from about 0.01 micron to about 1 micron into hair ducts on a section of skin and then illuminating the skin surface with light from a Nd:YAG laser. Generally the temperature of the contaminant is raised to 70° C to 80° C for about 0.1 second by this method. Energy transferred from the heated contaminant in the hair ducts to skin tissue surrounding the hair ducts provides long

term inhibition of hair growth in the hair ducts. Since the wavelength produced by a Nd:YAG laser penetrates skin with a minimum of absorption and scattering therein, overheating of surface skin tissue is avoided.

In another embodiment of the invention, the occlusive covering comprises a flat, flexible supporting scrim covered on one or both sides with a hydrogel. The scrim is generally a plastic lattice or cloth netting upon which the hydrogel is placed. The hydrogel is a three-dimensional polymeric network that can solvate a large quantity of water without dissolving. The copolymer can contain both hydrophilic and hydrophobic components. The hydrophilic monomers used are generally N-vinyl-2-pyrrolidone (VP), 2-hydroxyethyl methacrylate (HEMA), and 2 acryloylamido-2-methylpropanesulfonic acid (AMPS). Copolymerization with other hydrophobic monomers is generally carried out in the presence of crosslinking agents, such as divinyl benzene (DVB) and ethylene glycol dimethacrylate (EDMA). Examples of commercially available hydrogel-containing products suitable for use as an occlusive covering are as follows:

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<u>Product</u>	<u>Hydrogel Polymer</u>	<u>Supporting Scrim</u>
Second Skin®	Poly (ethylene Oxide)	polyethylene (PE) nonwoven scrim (Mfg. Spenco) interlayer with peelable polyethylene backing
CuraGel	HEMA:PEG:N=C-O	nonwoven cotton gauze on elastomer (Mfg. Kendall) substrate with PE backing
TTL Medical	HEMA:PEG:N=C-O	isolated nonwoven fibers. On elastomer (semi-occlusive urethane dressing) substrate with PE backing

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Hydrogels are composed mostly of water, for example greater than 80% by weight, immobilized in a matrix of a hydrophilic crosslinked polymer. One of the unique characteristics of hydrogels is that, due to crosslinking of the polymer system, they do not dissolve in the water they hold. The result is "trapped water" held by solvation to the hydrophilic portions of the hydrogel. To take advantage of these characteristics, when a hydrogel is used as the occlusive covering in the practice of this invention, it is usually not removed prior to

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lasing. Therefore, preferred hydrogels are those which provide optimal optical transmissivity and form a minimum of toxic products during lasing. Urethane gels may contain unreacted isocyanates, which have a distinct odor, and present a possibility that potentially hazardous pyrolites can be formed upon lasing, such as is formed by cleavage of common aromatic isocyanates. Consequently, the "urethane" type of HEMA:Poly(Ethylene Glycol):isocyanate hydrogel is useful, but poly (ethylene oxide) hydrogels are preferred if the hydrogel is to remain in place during lasing. Such PE hydrogels contain no hydrogen atoms and cannot form toxic by-products.

One of the advantages of leaving the hydrogel in place during lasing is to contain the contaminant and drive the contaminant downwards within the hair ducts. FIGS. 18A-18F illustrate how these advantages are achieved. If the occlusive dressing is removed, force vectors generated during lasing may spill the contaminant out of the hair follicle (shown in FIG. 18C).

During lasing a short pulse of energy vaporizes some of the contaminant, and a puff of smoke and fragments is produced, which fly off the skin surface as smoke or particles. In the present invention, the hydrogel serves as a blast barrier, to confine the smoke and fragments so formed. A particle or fragment in a hair duct is forced downward into the hair ducts (FIG. 18D). In addition, a portion of the water in the hydrogel evaporates, providing an additional instantaneous overpressure, shock, and acceleration to aid in propelling the chromophore into the depth of the follicle. Steam so created may instantaneously lift the hydrogel from the skin surface, but unvaporized water remaining in the hydrogel rapidly cools the laser-induced steam back to water, causing the hydrogel to "slap" against the skin surface. This "slap" may help propel the contaminant into hair follicles. Because the water content of the hydrogel is not compressible, it acts like a solid to the extent that it confines the force vectors of an exploding contaminant particle much in the same way that a sheet of plastic or glass placed over the skin surface prior to lasing would do (shown in FIG. 18E). Therefore, the hydrogel directs the energy of the ablation or explosion downward, helping to force the contaminant into the depths of the hair ducts (FIG. 18F).

The water in the hydrogel, which has a high specific heat, can absorb heat generated during lasing. As the hydrogel lies atop the skin to be treated, its heat absorbing properties

afford a unique means for preventing overheating of dermal tissue during laser hair removal techniques of all types. Further, it has been discovered that the hydrogel can be precooled or even frozen prior to application to the skin surface to provide an extra measure of cooling to the dermal tissue prior to the lasing phases of any hair removal procedures. A hydrogel dressing can be used to cool the skin surface whether the cooled or frozen occlusive dressing is removed during lasing or not. Studies have shown that light is satisfactorily transmitted through a hydrogel dressing when the hydrogel remains in place during lasing.

No. 4: A SOOTHING TOPICAL HYDROGEL DRESSING

Many patients experience some discomfort for a day or two following laser skin treatments, such as treatments for skin rejuvenation or to inhibit growth of hair. There are many types of prior art bandages and skin patches that can be applied to skin surfaces and which release active agents useful for reducing minor irritation, inflammation and pain. One such device disclosed in U.S. Patent No. 5,474,528 is a hydrogel skin patch that releases a photoactivated pharmaceutical agent to skin when illuminated with light, for example during laser therapy. However, it would be useful to have a hydrogel composition for application to skin that releases active agents for soothing and comforting irritated and inflamed skin without recourse to light energy. Such a composition would be particularly useful after laser therapy to reduce and/or alleviate irritations and inflammations.

The present invention is a soothing dressing for irritated skin comprising a cross-linked polymeric hydrogel matrix into which has been infused a hydrating agent, such as water, and an active agent useful for eliminating or alleviating a skin irritation, sensitivity or reddening. The hydrogel matrix can be made of any species of the wide classes of hydrogels, including but not limited to, polymers of acrylates, ethylene oxides of various molecular weights, vinylpyrrolidones, natural chitins, lectins, and various copolymers thereof. In one embodiment of the invention, the hydrogel matrix includes a sufficient amount of an adhesive hydrogel that the hydrogel dressing will self-adhere when applied to skin. U.S. Patent No. 5,143,071 to Keusch *et al.* cites an extensive list and description of prior art adhesive hydrogels that adhere to skin surface with an intimate physical contact. Generally, the polymeric hydrogel will contain up to 84 percent by weight of water when fully hydrated.

For example, the hydrogel can contain from about 60 percent to about 84 percent by weight of water, or from about 40 percent to about 60 percent by weight of water or other hydrating substance, such as an active agent in an aqueous solution.

The hydrogel dressing may further comprise a scrim with a hydrogel lining one or both sides of the scrim. The scrim is generally a plastic lattice or cloth netting for supporting the hydrogel, as described in Section No. 3 above. It is also contemplated that the hydrogel dressing can comprise two or more hydrogel layers bonded together along their faces, such as is described in Section No. 3. Such a scrimless composite hydrogel is more flexible than those with internal scrims and better suited to conform to body contours.

The hydrogel further comprises one or more of any type of active agent that would be beneficial for soothing and/or protecting reddened, irritated or inflamed skin. For example, the active agent can be an over-the-counter drug or folk remedy that serves as a mild antiseptic, an anti-inflammatory agent, or a topical anesthetic. Examples of useful active agents include benzocaine, hydrocortisone or hydrocortisone diacetate, aloe vera extract (available in freeze-dried form), and vitamin E. Rose oil is an example of a naturally soothing oil with a pleasant fragrance that can be added to the hydrogel as a perfume. Water soluble active agents are dissolved into water and the solution is used to hydrate the hydrogel. Oily active agents can be emulsified and the emulsion can be dispersed into an aqueous component for use in hydrating the hydrogel.

The soothing action of the active agents is greatly enhanced by effective delivery of the agents from the aqueous medium. Introduction of the active agent from the hydrogel into hydrated skin tissue, or through the hydrated stratum corneum, can be by diffusion, by absorption, or by any other mechanism constituting chemical permeation or penetration of the hydrated skin or stratum corneum. It is well established in the literature of chemical transport through skin that hydration can enhance the chemical transparency, transmissiveness, passage, or transport of pharmaceuticals through the stratum corneum. A review of the subject of enhanced transport of chemical agents across the stratum corneum in hydrated skin is found in Ghosh *et al.*, *Pharmaceutical Tech.*, April 1993, which is incorporated herein by reference.

When hydrated, the hydrogel dressing forms a thin relatively transparent layer on the skin surface. If the hydrogel layer that is placed against the skin is one of the mildly adhesive tacky hydrogels disclosed above, the hydrogel dressing is self-adhering and is relatively unobtrusive on the skin. This type of self adhesive hydrogel dressing is much less noticeable from a few feet away than a reddened mask of irritated skin. A tacky hydrogel will adhere to skin so that the dressing will continue to release the active agents over a period of many hours, for example about 8 to about 24 hours. Alternatively, any suitable adhesive known in the art can be used to affix the hydrogel dressing to a skin section to be treated so that it will remain in place until it is removed by the patient, or falls apart in the shower or by wear and tear. However, care should be taken that as much as possible of the outer surface of the hydrogel dressing is not covered by the adhesive, but is exposed to the ambient air during the time the dressing is worn by the patient. With this precaution, the hydrogel dressing will administer the soothing active agent(s) to the skin to be treated over an extended period of time in slow release as the water in the hydrated hydrogel slowly evaporates due to contact with ambient air and the body heat of the patient. Natural evaporation of water from the hydrogel dressing, which can be re-wet from time to time, provides an additional cooling and soothing effect to irritated skin.

The hydrogel dressing of this invention provides an improved slow release vehicle for administration of soothing active agents to a skin surface without application of light to the dressing. The dressing is less obtrusive visually than standard gauze and tape dressings, and is specifically designed to be used following cosmetic laser skin treatments, such as treatments for hair removal or skin rejuvenation.

No. 5: EXPOSURE-INDICATING HYDROGEL COMPOSITE FOR LASER APPLICATIONS

During application of a laser to a skin or tissue surface, certain cell particles and pathogens contained in the treated tissue, such as viral particles, may become air-borne. In addition, some degree of smoke and/or odor may be produced. It is known to cover the tissue to be lased with a transparent film or hydrogel to reduce the level of air-borne skin products

that may put the laser operator at risk. However, such coverings obscure the treatment site so that it is difficult to see and keep track of which areas have been treated and which have not.

The present invention provides a scrim-less hydrogel with an exposure-indicating layer for covering a surface area to be treated by laser. Hydrogels, being mostly water, are fragile and have little tear strength. In certain hydrogels, a supporting scrim, which is usually a plastic lattice or cloth netting, provides a structure upon which the hydrogel is placed, along one or both sides. The supporting structure within these prior art hydrogel compositions absorbs some energy from the laser. More importantly, the interior scrim limits the elastic modulus of the hydrogel and, hence, its ability to conform well to the contours of a body upon which it is placed for use as a covering.

In the present invention, the supporting interior scrim is eliminated to reduce laser energy absorbed by the composite hydrogel, for example, when laser energy is administered to a skin or tissue surface covered by the composition to reduce air-borne particles and/or to aid in propulsion of a contaminant into hair ducts. Rather than having an interior scrim, the composite hydrogel of the present invention contains at least two hydrogel layers firmly attached or bonded together along their faces. The attachment can be of any type that forms a substantially transparent bond between the two hydrogel layers, for example by lamination. It is preferred that the bond between the hydrogel layers have an absorbance coefficient of no more than about 1% to about 5%, or an optical transmission of from about 95% to about 99%.

The composite hydrogel is described with reference to FIG.19A as follows. The hydrogel composite 22 comprises at least two hydrogel layers. One of the two layers is a film 24 of a thermoplastic or solution-cast hydrogel polymer with fewer hydrophile sites in its architecture than is used for the material which comprises the bulk of the laminate, the hydrogel layer. The hydrogel film is selected to allow a maximum water uptake or swelling of about 15% to about 25% by weight. The composition of the thermoplastic hydrogel film is selected to provide tear strength to the composite hydrogel sufficient to withstand application of the composite to a contoured body surface while maximizing the elastic modulus of the composition. The second of the two layers is a layer 26 of crosslinked polymeric hydrogel. Such crosslinked polymeric hydrogels will typically hydrate and swell to a water content of

about 75 percent to about 95 percent by weight of water. One face of the thermoplastic hydrogel film and of the polymeric hydrogel layer are permanently attached or bonded together so as to minimize the light absorbence at the bond 28.

The thermoplastic hydrogel layer is referred to as a "film" while the cross-linked polymeric hydrogel is referred to as a "layer" to indicate the relative thickness of the two layers. Generally the film is no greater in thickness than is required to hold the composite hydrogel together during use. Excess thickness in the thermoplastic hydrogel will impair the flexibility of the composite and its ability to conform readily to contoured body surfaces. Generally, the total thickness of the composite hydrogel is in the range from about 2 mm to about 5 mm.

To indicate the track of the laser beam over the surface of the hydrogel composite during use, in one embodiment shown in FIG. 19 the exterior surface of the thermoplastic hydrogel film (*i.e.*, the one not attached to the layer of crosslinked polymeric hydrogel) has a coating 30 of an indicator material. The coating can be partial, for example in a discontinuous or openwork pattern. Alternatively, the coating can be eliminated if the hydrogel film incorporates an indicator material such as a photoactivated dye or chemical. The indicator material is selected to change color upon illumination with at least one frequency of light, such as is provided by a laser. For use with any known laser, the indicator material is selected to change appearance, for example, change color, when subjected to the light of the laser to be used.

The indicator material and its pattern of coating should be selected to perform its indicator function while absorbing a minimal amount of light energy. For example, the coating of indicator material can be a partially metallized surface, such as is formed by vacuum evaporation of aluminum or other metal space. It has been found that vapor-deposited metal films, for example of aluminum or vacuum-coated bismuth, change appearance when illuminated by infrared such as is provided by a Nd:YAG laser at a wavelength of about 1 micron.

The indicator material can also be a photoresponsive pigment, such as iron oxide, rhodamine red, or phthalocyanine blue, printed over the exterior surface of the thermoplastic hydrogel layer in an open-work pattern, such as a pattern of dots 32, intersecting lines 37, or

cross-hatched lines 39, as shown in FIG. 19B. Certain pigments, such as Monastral Blue™ (phthalocyanine) and bismuth trioxide will react to infrared light. Monastral Blue™ pigment also changes appearance when illuminated by light in the visible region, for example under the red light of a ruby laser. Bismuth trioxide or bismuth subcarbonate, rather than being
5 “bleached” by the laser energy, are reduced to the metal by the light, resulting in a darkening of the lased area. This phenomenon can be beneficial for blocking exposure of the lased area of skin upon subsequent passes of the laser, if desired.

To minimize the laser absorption of the open-work pattern, it can be printed in a half-tone, for example a fine half-tone. Generally the ratio of the surface area covered by the
10 indicator material to that not covered by the indicator material (*e.g.*, the open spaces between the dots) is in the range from about 1:5 to about 1:10. It is preferred that the area not covered by the indicator material be about 90%, or more, to allow visualization of the laser-affected areas while minimizing attenuation of the therapeutic radiation. The object is to deposit only enough indicator material on the surface of the hydrogel film to be visible to an operator, but
15 not enough to substantially reduce the therapeutic radiation reaching the patient.

Examples of crosslinked polymeric hydrogels and thermoplastic hydrogels suitable for use in making the thin film 24 of the composite hydrogel include elastomeric polymers, such as polyurethane, having hydrophilic sites in the polymer molecule of polyethylene glycol and a molecular weight of less than about 1,000 units, for example from about 400 to
20 about 600 units. The supporting film does not imbibe as much water as hydrogel layer 26, but retains its ability to transport water to the air, allowing some evaporative cooling and oxygen transfer to take place. Examples of hydrogels suitable for making layer 26 of the composite hydrogel include any of the commercial classes of hydrogels, such as the urethane type having hydrophilic sites comprising polyethylene oxide and a molecular weight of from
25 about 1,000 to about 2,000 units. Alternatively, any of the common commercial classes of hydrogels can be used for layer 26, such as a hydroxyethyl methacrylate or a electron-beam crosslinked high-water content polyethylene oxide hydrogel, such as is sold by Thermedics, Inc., Woburn, MA. Generally the hydrogel used for making layer 26 is capable of imbibing greater than about 80% by weight of water. Because of supporting film 24, certain tear-
30 resistant polyethylene oxide types of hydrogel that have not been cross-linked by an electron

beam have been used in prototypes of these laminates. Due to the high water content of layer 26, the composite hydrogel is flexible and readily conforms to body contours.

The water imbibed by the hydrogel composite can optionally contain an active agent for alleviating pain, reducing irradiation, *etc.* During use, laser irradiation will aid in releasing the soothing active agent to the skin surface. Examples of active agents useful for soothing skin are described in Section No. 3 of this application.

Methods of making hydrogel compositions are known in the art and are not repeated herein. One skilled in the art can readily modify existing methods to fabricate the exposure-indicating hydrogel composite of this invention. For example, in one embodiment, the composite hydrogel is obtained by a method comprising the following steps. A film is extruded of one or a combination of thermoplastic hydrogel polymers that typically hydrate and swell to contain a water content of about 15% to about 25% by weight of water. The extruded film is laminated to a preformed layer of a crosslinked polymeric hydrogel that will hydrate and swell to contain a water content of about 75 % to about 95 % by weight of water. The remaining free surface of the thermoplastic hydrogel film is coated in an open work pattern with an indicator material that changes appearance upon laser irradiation, but absorbs a minimal amount of light energy. If the indicator material is a metallic substance, such as aluminum, the coating can be applied using a technique of vacuum evaporation. If the indicator material is a photoresponsive pigment, such as iron oxide, rhodamine red, or phthalocyanine blue, the coating can be printed in an open-work pattern, such as a pattern of dots or intersecting lines. One skilled in the art will be able to select an indicator material that is activated by the light of the particular laser wavelength desired for use in a skin treatment process. All that is required is that the indicator material change appearance when illuminated by a laser with the particular wavelength of light selected for use without being completely photo-ablated from the surface of the composite hydrogel.

In use, the exposure-indicating hydrogel composites of this invention are hydrated and placed over a skin surface for laser treatment, with the free surface of the crosslinked polymeric hydrogel layer against the surface of the skin. The surface of the composite with the coating of indicator material does not contact the skin surface, but faces away, so that the indicator material can be readily seen by a laser operator. A light beam to be applied to a skin

surface is transmitted through the hydrogel composite to a skin surface with which it is in contact. As the light of the light beam strikes the indicator material, the track of the beam causes a photoactivated change of appearance in the indicator material. As a result, an operator can readily determine exactly which areas of the skin or other tissue covered by the hydrogel composite have been treated by the light beam. The hydrogel composites are particularly well suited for use as an occlusive dressing in the methods described in Section No. 3 above, in which the occlusive dressing aids in propulsion of chromophore particles into hair ducts and other skin structures.

When hydrated and placed over a skin surface prior to treatment with a light beam, the exposure-indicating hydrogel composites described herein cool the skin surface by evaporation of water from the hydrogel, and prevent generation of air-borne particles of tissue. In addition, they absorb less light energy and conform more readily to body contours than do hydrogels that contain an interior scrim. Due to a photoactivated appearance change caused by the laser in the indicator coating, such as a color change, these compositions offer the additional advantage of recording the track of the laser over the skin surface to aid the laser operator in keeping track of which areas have been treated, and which have not. In methods of hair removal or skin rejuvenation, these composite hydrogels can also be used to aid in the propulsion of chromophore particles into hair ducts for use in inhibiting hair growth, or beneath surface skin cells to be removed in skin peeling operations.

No. 6: A METHOD FOR CONTROLLING THERMAL AND MECHANICAL DAMAGE DURING LASER HAIR REMOVAL BY SELECTING CHROMOPHORE PARTICLE SIZE

Hair removal techniques are known that rely upon the transfer of heat energy to hair follicles to inhibit hair growth. By raising the temperature of tissue surrounding the hair ducts and maintaining it at the elevated temperature for a sufficient period of time, the target tissue is destroyed, *e.g.*, by thermal coagulation of the hair follicle and of tiny blood vessels that nourish the follicle.

In laser treatments to inhibit hair growth, it is known to infiltrate a contaminant containing light-absorbing chromophore particles into hair ducts, and then illuminate the skin

surface containing the contaminant-filled hair ducts with short pulses of light at a wavelength absorbed by the contaminant. Chromophore particles absorb short pulses of high energy light and either explode, releasing the energy in the thermal and mechanical forms, or do not explode and transfer the absorbed energy in the form of heat to surrounding tissues by thermal conduction. It would be advantageous to control the delivery of mechanical and/or thermal damage to the tissue surrounding hair ducts with the goal of inhibiting future growth of unwanted hair while avoiding significant damage to the surface of the skin.

Whether pulses of light having a given pulse duration and fluence will cause a chromophore particle to explode or heat up depends upon the size of the particle. In one embodiment of the invention, the chromophore particle size is selected to preferentially induce either thermal or mechanical damage to the tissue surrounding hair ducts into which a contaminant containing chromophore particles is infiltrated for use in a hair removal procedure. In other embodiments, the particles in the contaminant have two different sizes or a bimodal size distribution with the portion of larger particles determining the proportion of mechanical damage desired and the portion of smaller particles determining the proportion of thermal damage desired.

The practical upper limit on the size of chromophore particles used for infiltration into hair ducts to effect hair removal is the diameter of a hair duct, which is from about 70 μm to about 1 micron for human hairs. If a hair duct contains a hair, even smaller particles are generally used. Another practical consideration that affects the size of particles used in hair removal techniques is the prohibitively high cost of manufacturing uniformly sized particles in the submicron size range, such as uniformly sized carbon particles. Generally, for this reason, particles in this size range are obtained by grinding larger particles. The result is particles having a range of sizes, rather than uniformly sized particles. Even if the particles are uniform in diameter, due to their small size, they tend to clump together in aggregates. For example, the fullerene molecule (C_{60}) has the shape of a soccer ball with a calculated diameter of about 0.7 nm, but aggregates of C_{60} reach 200 μm in size. Therefore, chromophore particles used in hair removal generally have a wide size distribution, generally in the range from about 0.01 μm to about 1 μm .

Carbon in the forms of graphite, carbon black, and fullerene is an excellent photon absorber and is available in particles having a wide range of sizes. Fullerene is available in particles or aggregates ranging in size from about 0.7 nm to 200 μm in size. Particles of carbon black range from about 10 nm to 500 nm in diameter, depending on the method of production. Graphite can be ground to form particles having a wide size distribution with an average size down to one micron. Particles can also be powder, or even pure carbon dust in one extreme. Any of these micro-particles of carbon can be loaded into hair follicles, whose diameter for human hairs is in the range from about 100 μm to 10 microns.

A contaminant with a bimodal size distribution is readily obtained by mixing together two groups of particles with different modal distributions, one relatively larger, and one relatively smaller.

In general, light absorbing chromophore particles of a relatively larger size will vaporize or explode when illuminated with at least one short pulse of light at sufficiently high power and a sufficiently short pulse duration. A consequence of vaporization is the shattering of the particle, with propulsion of the fragments into the depths of the hair follicle and into the surrounding cells. While vaporization of the contaminant particles is highly desirable for forcing the contaminant particles into the bottom of hair ducts, the most significant damage particles of this size can impart to tissue is cellular damage resulting from direct photomechanical disruption of the cellular membrane and other cellular structures. When the exploding particles are confined within a hair duct, the membranes of cells adjacent to the exploding chromophore are disrupted by the shock wave and by the exploded fragments of the particle bombarding the surrounding cells. The photomechanical effect of utilizing the larger size particles can be enhanced by using pulses in the nanosecond range of duration, for example about 1 to about 20 nanoseconds.

Other factors that influence whether a chromophore particle will explode or merely heat up when irradiated with short pulses of light of given pulse duration, frequency and fluence, are the physical properties of the particular chromophore used, such as its latent heat of vaporization and photon absorption coefficient. The photon absorption coefficient of graphite when irradiated with light having a wavelength of 1064 nm is estimated to be from about $1 \times 10^5 \text{ cm}^{-1}$ to $2 \times 10^4 \text{ cm}^{-1}$ (T. Barrett, *Absorption of Light by Small Spherical*

Particles in a Liquid, ThermoTrex Corporation and T. Barrett, *Handbook of Carbon, Graphite, Diamond and Fullerenes*, Noyes Publications, Park Ridge, N.J., 1993). The corresponding depths to which the light will penetrate in a carbon particle before its energy has been absorbed, (*i.e.*, the light penetration depth in carbon corresponding to the above
5 range of photon absorption coefficients) is from about 0.1 μm to about 0.5 μm , respectively.

The present invention is illustrated with reference to particles of carbon, but other chromophore particles that absorb light and do not form toxic byproducts when pyrolyzed in hair ducts can also be used, and their use is specifically contemplated to be within the scope of this invention. One skilled in the art will appreciate that, if the heat of vaporization and
10 absorption coefficient of a chromophore is known, thermodynamic principles can be used as illustrated herein to calculate what size range of particles will vaporize, and what size range will heat up and transfer heat to surrounding tissue without the loss of energy associated with vaporization of the particles.

The invention is more particularly described with reference to carbon particles as
15 follows. In a hair follicle, carbon particles with an average diameter of approximately 1.0 micron will vaporize when illuminated via a Nd:YAG laser having a light beam with an energy density of about 2.5 J/cm², and a pulse duration of about 10 nanoseconds. These explosions translate mechanical energy to kinetic energy in the form of a shockwave, which causes both heat and motion. It has been discovered that the shockwave caused by exploding
20 chromophore particles contributes substantially to the damage to the skin tissue that feeds growing hair follicles. Thus, an important aspect of the present invention is selection of chromophores having a particle size that will readily explode under the type of illumination provided, *i.e.*, the energy density of individual pulses and the length of the pulse duration.

By contrast, relatively smaller particles of chromophore illuminated by pulses of light
25 at the same power and pulse duration will tend not to explode, but will rapidly release the heat they absorb to a surrounding medium by thermal conduction. When the relatively smaller particles are confined within a hair duct, heat is rapidly conducted from the heated particles to the surrounding skin tissue, thereby causing thermal damage to such tissue. The thermal effects of illuminating the smaller particles may be increased by prolonging the pulse
30 duration of the laser to the microsecond or millisecond range. For instance carbon particles

with an average diameter in the range from about 1 to 50 nanometers will transfer absorbed heat to a surrounding medium such as skin tissue, substantially without explosion or vaporization when illuminated under the same conditions that explode 1 micron particles (*i.e.*, a Nd:YAG laser with a fluence of about 2.5 J/cm^2 and a pulse duration of about 10 ns).

5 FIGS. 20A-C illustrate these concepts schematically. FIG. 20A schematically represents the transfer of photothermal energy to tissue surrounding a hair follicle 31 infiltrated with contaminant 14 containing carbon particles with diameters in the 1.0 to 50 nanometer range and illuminated by Nd:YAG laser light beam 7. FIG 20B schematically represents the transfer of photomechanical energy to tissue surrounding a hair follicle 31
10 infiltrated with contaminant 14 containing carbon particles with diameters of about 1.0 micron and illuminated by Nd:YAG laser light beam 7. FIG. 20C schematically represents the combined transfer of photomechanical and photothermal energy to tissue surrounding a hair follicle 31 infiltrated with a combination of the contaminant carbon particles of FIGS. 20A and 20B.

15 Due to the extraordinary amount of energy that is consumed in transforming solid particles to a gaseous state, vaporization of particles consumes a large portion of the energy delivered to the particles. By comparison, heating the particles is very energy efficient. For example, about 7,686 J per gram will heat graphite from 0°C to 3700°C , its vaporization temperature, but about 10 times as much energy is required to vaporize graphite, or about
20 65,000 J per gram. Therefore, much more powerful light pulses are needed to vaporize graphite and utilize photomechanical damage than is required for a purely thermal effect.

Vaporization of the chromophore particles is particularly useful for generating a force to propel the particles and their fragments deep into hair ducts and the walls of hair follicles. Once propelled into the vicinity of hair papillae, continued explosion of the particles by the
25 pulses of light will produce shock waves and rapidly propel fragments so as to cause damage to hair growth cells responsible for the production of hair shafts. The damage inflicted on hair growth cells by these photomechanical effects may extend hundreds of microns into the walls of follicles.

In one embodiment of the laser hair removal method, vaporization of the carbon
30 particles is required to generate a force propelling the particles and their fragments deep into

hair ducts and the walls of hair follicles. Once located in the vicinity of the hair papilla and the structures responsible for production of the hair shaft (hair growth cells), the particles can be exploded again and again by the laser pulses to produce shock waves and rapidly moving fragments that will damage surrounding tissue. The damage to surrounding tissue by these photomechanical effects may extend hundreds of microns into the walls of the follicles. The acoustic shock waves being transmitted at the speed of sound will propagate substantially deeper and faster than the thermal damage at the short 10ns pulse duration. Once shattered by explosion, large particles and aggregates will end up as a collection of much smaller fragments, which will absorb light energy and transfer heat into tissue without much mechanical damage.

In order to thermally devitalize cells in tissue surrounding a hair follicle, the tissue needs to be maintained at a high temperature for a period of time that varies with the temperature. The higher the temperature, the shorter the period required. For example, at 45° C, the required duration is about a couple of hours. However, it takes only about 0.1 second to damage skin cells at 70° C, and only about 1 millisecond at 80° C. The temperature to which a chromophore particle will be raised by any given pulse duration and laser fluence as well as the amount of heat it will deliver to surrounding tissue depends upon the thermodynamic properties of the chromophore, and the size of the chromophore particle irradiated.

The combination of mechanical and thermal energy transferred from the particles to the skin tissue sought to be destroyed is a very effective technique for achieving long term inhibition of the growth of hairs in hair ducts. Simultaneous photothermal and photomechanical damage to hair follicles is obtained by infiltrating into hair follicles a contaminant that contains a mixture of two particle sizes. For example, a contaminant containing a mixture of carbon particles having a diameter of about 1 nm to about 50 nm, for example about 10 nm, and carbon particles having a diameter of about 3000nm to about 500nm, for example about 1000 nm, can be used to induce simultaneous mechanical and thermal damage to skin tissue surrounding hair ducts.

The contaminant can further include a liquid, such as an oil, surfactant, or water-based lotion. In all mixtures and/or suspensions of chromophore particles in a suitable liquid, as well as solutions in which the carbon, or other chromophore, particles are dissolved in a

solvent, the liquid acts as a heat sink for a vaporized particle, and causes the vaporized particle to condense back into the solid phase with the release of its heat of sublimation. For example, at a dilution of less than 1% by volume of 1 micron sized carbon particles in oil, the particles may shatter and vaporize to gaseous carbon, as well as emit smaller carbon particles.

5 The oil is correspondingly heated, and transfers its heat to nearby cells. Therefore, an oil-containing contaminant with concentrations of carbon particles less than about 20% by volume (such as 2, 0.2 or even 0.02 volume %) increases the proportion of photothermal damage to the skin cells surrounding hair ducts, at the expense of photomechanical damage that would otherwise be caused by the particles alone. Also, rapidly moving solid carbon
10 particles tend to be slowed down by the oil, thus lessening or preventing mechanical damage. Therefore, the proportion of mechanical to thermal damage caused in the hair follicles can also be controlled by varying the overall concentration or amount of the chromophore particles in the contaminant. For any given chromophore particle size and laser pulse width, there will be an optimum concentration of the light-absorbing chromophore in the mixture.
15 Too much chromophore content (*e.g.*, carbon particles) will act as a heat sink as well as block the passage of photons. Too little chromophore content will not absorb enough light, and will not heat up enough to effectively damage adjacent cells.

In the case of a contaminant having chromophore particles with a substantial range of sizes (as is obtained by grinding large particles to obtain smaller particles), the proportion of
20 photomechanical to photothermal damage caused to the skin cells surrounding the hair ducts by the particles infiltrated therein can be controlled by controlling the size distribution of the particles and/or the average size of the particles. In general, decreasing the average size of the particles, decreases the proportion of photomechanical to photothermal damage, and increasing the average size of the particles increases the proportion of photomechanical to
25 photothermal damage. Similarly, when the distribution of particles having a range of sizes is skewed towards the relatively larger particles, a larger proportion of mechanical damage will be obtained than when the distribution is skewed towards the relatively smaller particles.

In one embodiment of the invention, the particles infiltrated into hair ducts have a varied major dimension selected so that a combination of photomechanical and photothermal
30 damage can be simultaneously administered to skin tissue adjacent to the hair duct, even

when the pulse duration and the fluence of the pulses of light are held constant. It is generally desirable that no more than about 20 to about 5 percent of the energy delivered by the light source should be expended in vaporization of particles. Therefore, in one embodiment of the invention, wherein carbon is the chromophore, from about 10 to about 30 percent by weight of the particles have a major dimension in the size range from about 3000nm to 500nm, and the balance of the particles have a major dimension in the size range from about 500nm to 100nm. Similarly, by proper selection of the proportion of the particles that fall into the smaller and the larger size ranges, the proportion of photomechanical to photothermal damage caused upon illumination of the particles at any fixed fluence can be controlled.

The hair removal procedure may also be divided into two or more phases, including a first phase during which the contaminant is irradiated so as to explode the particles to drive them into the depths of the hair follicles, (*i.e.*, the propulsion phase) and a second phase during which the contaminant is irradiated so as to raise the temperature of the tissue immediately surrounding the hair follicles to cause sufficient damage to inhibit future hair growth (*i.e.*, the thermal phase). Such a procedure is described in co-pending U.S. Patent Application Serial No. 08/644,231, filed May 13, 1996, which is incorporated herein in its entirety. For use in a multi-phase hair removal procedure of this type, during the first phase a majority of the carbon particles have an average diameter in the range from about 1 to about 60 nanometers, for example, about 10 nm, to maximize the proportion of photothermal damage effected. Then, during the second phase of the illumination, to maximize the proportion of photomechanical damage caused by illumination of the particles, the majority of the particles have an average diameter in the range from about 3000nm to 500nm, for example about 1000 nm. These size ranges are particularly preferred when the chromophore particles are carbon and the illumination is by pulses of light about 10 nanoseconds in duration with a wavelength of about 1.06 micron. One skilled in the art will be able to adjust the size ranges to correspond to alternative chromophores, wavelengths of light, and pulse length using thermodynamic calculations.

The present invention provides improvements in known methods of laser hair removal procedures. It allows the practitioner to control the thermal and/or mechanical damage administered to hair follicles either simultaneously or in sequential phases, by

selection of the size of particles in a contaminant infiltrated into hair ducts. The practitioner is afforded increased control over the difficult task of forcing chromophore particles into the depths of hair ducts using laser light. The invention also affords the practitioner improved control over the amount of heat that is administered to the tissue in and surrounding the hair follicles during lasing. As a result of these improvements, the risk of unwanted damage to skin tissue is lessened, while the techniques of inhibiting hair growth are improved.

No. 7: A METHOD FOR CONTROLLING PHOTOMECHANICAL VERSUS PHOTOTHERMAL DAMAGE DURING LASER HAIR REMOVAL BY SELECTING PULSE DURATION

The use of a laser to induce hair follicle damage via irradiation of a carbon chromophore (*e.g.*, carbon particles) has been previously described. The purpose of this invention is to employ modulation of and/or combinations of laser pulse durations to control administration of photomechanical and/or photothermal damage to the hair cells via an exogenous chromophore infiltrated into hair ducts.

The effect of particle size in controlling whether photomechanical or photothermal damage is administered to hair follicles by means of chromophore particles infiltrated therein is disclosed in Section No. 6 above. It is also possible to achieve a combination of mechanical and thermal damage to tissue surrounding hair ducts by using a relatively homogeneous size of particles, in conjunction with a combination of relatively long and short pulses of light. In general, short pulses of light tend to explode a chromophore particle, thus causing photomechanical damage. Pulses having a pulse width longer than the thermal relaxation time of a particle tend to heat up a particle without explosion so that heat is transferred to a surrounding medium. The surrounding medium is skin tissue surrounding a hair duct and/or a liquid medium in which the particle is dissolved or suspended. Thus, photothermal damage is caused to tissues adjacent to chromophore particles radiated by relatively long pulses of light. The combination of long and short pulses can be an alternating pattern of long and short pulses, a succession of short pulses followed by a succession of long pulses, or *vice versa*, or the long and short pulses can be administered simultaneously. In the latter case, it may be convenient to utilize two lasers simultaneously.

As used herein, the terms “long” and “short” are relative terms and must be defined with reference to the type and size of the chromophore particles illuminated. This principle is illustrated herein with reference to carbon particles and light pulses provided by a Nd:YAG laser with pulse frequency of about 10 Hz and fluence of about 2 to about 3 J/cm². Under these conditions, a “short” pulse duration (of a Nd:YAG laser) will be from about 10 ns to about 30 ns, while a “long” pulse duration will be from about 100 μ s to about 100 ms. Preferably the carbon particles are suspended in an oil or water medium. Irradiation of the carbon with a “short” pulse will: a) break up aggregates of carbon particles, b) induce shattering of the larger (>50 nm) particles into smaller particles, c) drive particles deeper into the hair shaft due to the explosive force of the shattering of particles, and d) cause vaporization of the carbon to induce photomechanical tissue damage. A “long” pulse, on the other hand, will lead to heating of the smaller carbon particles, and the heat will be transferred (*e.g.*, via an oil medium) to the surrounding tissue to induce photothermal damage, but will substantially avoid exploding or vaporizing the particles.

One option for producing both photothermal and photomechanical damage to the follicular tissue is to alternate short and long pulse durations when illuminating chromophore particles infiltrated into hair ducts. Alternating the pulse duration between short and long pulses will serve to break up any aggregates of carbon particles, and will cause both photomechanical and photothermal damage to tissue surrounding hair ducts into which the particles have been infiltrated.

The following examples model a zero-order estimation of the laser parameters suitable for administering any desired combination of photomechanical and photothermal thermal damage to hair follicles without burning skin, coagulating blood vessels in the dermal matrix, or destroying the skin pigment (*i.e.* melanin) located at the interface of epidermis and dermis.

Example 4

Short vs. Long pulse Lasers

The laser pulse energy and duration give rise respectively to the amount and rate of energy absorbed in light-absorbing chromophores respectively. For a given energy, the

shorter the pulse duration, the higher the temperature rise in the light-absorbing medium. The absorbed energy is confined well inside the light absorbing chromophore at the end of a short duration pulse. Conversely, much of the heat may be dissipated into the surrounding medium if the pulse duration is very long. As a zero-order approximation, the energy dissipation distance in a given period of time can be written as:

$$x = \sqrt{\alpha\tau} \quad (1)$$

where x in cm is the energy dissipation distance; τ in *seconds* is the duration of energy dissipation; α in cm^2/sec is the thermal diffusivity, which is determined by the mathematic expression $\alpha = K/\rho c$ in which K is in $J\ cm^{-1}\ s^{-1}\ ^\circ C^{-1}$, ρ is in g/cm^3 , and c is in $J\ g^{-1}\ ^\circ C^{-1}$, represent the thermal conductivity, density, and thermal capacity, respectively. Table 4 lists the energy dissipation distances in graphite, mineral oil, and skin during a period of 10 ns (typical Q-switched Nd:YAG laser pulse duration), 100 μs (typical duration of non-Q-switched or free running Nd:YAG laser), and 100 ms (the duration between pulses of a 10 HZ laser). Table 4 shows that for a 1 μm graphite particle suspended in mineral oil or a 1 μm melanosome in skin, the absorbed energy is confined well inside the particle at the end of a 10 “short” ns pulse, but dissipates a significant distance from the particle during a “long” 100 μs pulse.

Table 4

The energy dissipation distance X (μm) in graphite, mineral oil, & skin during period τ

τ	X_{GRAPHITE}	X_{OIL}	X_{SKIN}
10 ns	0.16	0.03	0.03
100 μs	16.3	2.82	3.23
100 ms	515	89.1	102

Note: the thermal diffusivities (cm^2s^{-1}) used in the calculation for graphite, mineral oil, and skin are 0.027, 7.94×10^{-4} , and 0.001, respectively

Neglecting the energy loss due to dissipation, the instantaneous temperature rise in a light absorbing medium at the end of a 10 ns laser illumination can be expressed as

$$\Delta T = \frac{\mu_a \phi}{\rho c} \quad (2)$$

where μ_a in cm^{-1} is the absorption coefficient; and ϕ in J/cm^2 is the laser fluence. Because of the high absorption coefficient of graphite, its instantaneous temperature rise is over $1000^\circ C$ even at a $0.1 J/cm^2$ laser fluence. The vaporization temperature of graphite (about $3700^\circ C$) is reached at about $0.3 J/cm^2$. For purposes of thermal coagulation of the hair follicle, vaporization of light absorbers should be avoided. It takes about 7,686 J per gram to heat graphite from $0^\circ C$ to $3700^\circ C$, but it needs about 9 to 10 times more energy to vaporize graphite (about 65,000J per gram). It is estimated that only about 5% of the energy needed to vaporize graphite is converted into kinetic energy of the vapor. Thus, about 95% of the laser energy cannot be used to raise the temperature of the tissue to be thermally damaged. Therefore, a Q-switched short pulse laser is not a good choice in terms of thermal damage of tissue. For graphite particles whose size is small enough so that the energy dissipation is significant even during a 10 ns pulse duration, vaporization of these particles can be prevented as was demonstrated for the situation of 1nm and 10 nm graphite particles suspended in mineral oil. However, this scenario is hard to be implemented in practice because small particles tend to group together. For example, while a single C_{60} fullerene is only about 1 nm in diameter, the aggregates of C_{60} fullerene can be as large as $300 \mu m$ across. Furthermore, longer pulse duration is required in order to prevent burning of the skin, damaging blood vessels, destroying the skin pigmentation, *i.e.*, the melanosomes.

For pulse durations longer than $100 \mu s$, the energy deposited in a light absorbing chromophore can spread out significantly and thus reduce the peak temperature rise of the chromophore. As shown in Table 4, during a $100 \mu s$ period, the energy spreads out about $16 \mu m$ in graphite and about $3 \mu m$ in mineral oil. With respect to the photon penetration depth of about $0.1 \mu m$ in graphite at 1064 nm, the absorbed energy dissipates very far away from the source. For $1 \mu m$ graphite particles suspended in mineral oil, the temperature rise of the particle at the end of $100 \mu s$ illumination period with $1 J/cm^2$ fluence is about $450^\circ C$. At the same fluence, the instantaneous temperature rise without energy dissipation would be over

10,000° C if vaporization did not take place. A long pulse laser is clearly the choice to effect thermal damage of hair follicles. Even a 100 μ s pulse is not long enough for some situations, as demonstrated below.

5

Example 5

Thermal "Heating" of Hair Follicle with Long Pulse Laser

The temperature rise in the light absorbing chromophore and the surrounding medium can be obtained by solving the heat conduction equation:

$$K\nabla^2 T + S = \rho c \frac{\partial T}{\partial \tau} \quad (3)$$

10 where the first term is the energy flow rate into a unit volume due to a temperature gradient with K representing thermal conductivity; the second term represents the energy production rate per unit volume by heat source; and the term on the right side of the equation represents the energy associated with the temperature change per unit volume per unit time. With boundary and initial conditions given, the above equation can be solved to give the temporal and spatial distribution of temperature.

15 For the case of a hair follicle filled with light absorbing chromophores, analytical expressions of the temperature inside the hair follicle and in the surrounding tissue can be obtained with the following approximations (H. S. Carslaw *et al.*, *Conduction of Heat in Solids*, Oxford University Press, N.Y., 1995, p 347):

- The hair follicle is considered as an infinitely long cylinder.
- 20 • The light absorbing medium inside the follicle and the surrounding tissue are different uniform substances, but with the same initial temperature T_0 .
- There is a constant heat production S per unit time per unit volume at $t > 0$ inside the cylinder.

25 The temperature rise during heating and thermal relaxation after heating are related by:

$$\Delta T(r,t) = \begin{cases} \Delta T_1(r,t) & 0 \leq t < \tau_p \\ \Delta T_1(r,t) - \Delta T_1(r,t-\tau_p) & t \geq \tau_p \end{cases} \quad (4)$$

where $\Delta T_1(r, t)$ and $\Delta T(r, t)$ represent the temperature change during and after the heating phase, respectively; τ_p is the duration of heating; and r and t denote the radial coordinate and time, respectively. The thermal conductivities and diffusivities of the two media inside and outside the cylinder need to be known in order to calculate the temperature change for hair follicles filled with a topically applied contaminant comprising micron size graphite particles suspended in mineral oil with a mass ratio of 20%. These quantities in the contaminant are determined by the properties of graphite, mineral oil, and their volumetric ratio, using known procedures.

For heating of a graphite suspension in mineral oil with laser pulse longer than 100 μs , it is possible to heat up the lotion fairly uniformly because of the energy dissipation from graphite particles to mineral oil. Assuming a constant laser fluence reaching a hair follicle and absorption in the follicles of all the photons striking it, the heat production per unit volume per unit time is determined by formula 1.5 as follows:

$$S = 2 \frac{\phi}{\alpha \tau_p} \quad (5)$$

where S ($J cm^{-3} s^{-1}$) is the heat production per unit volume per unit time; ϕ (J/cm^2) is the laser fluence striking the hair follicle; α (cm) represents the radius of the hair follicle; and τ_p (sec) denotes the pulse duration.

With the treatments discussed above, the temperature distribution $T(r,t)$ for the case of a hair follicle filled with graphite/oil contaminant are calculated for different laser fluences and pulse durations. Immediately after the laser pulse, the energy is localized well inside the hair follicle, but the temperature of the lotion is well below the vaporization temperature of graphite (about 3700° C). By 10 ms after irradiation, the hair follicle is appreciably thermally relaxed. To demonstrate the pulse duration effect, the laser fluence is kept at 3 J/cm², but the pulse duration is stretched from 100 μs to 10 ms. For pulse durations from 100 μs to 10 ms,

the temperature rise of the tissue between the wall of a follicle and a distance one follicle radius away from the wall is over 50° C for a period of a few milliseconds. The corresponding absolute temperature is over 80° C after adding on the base body temperature (about 37° C).

5 Tissue is damaged if kept at 80° C for a period of about 1 ms. Thus, the tissue as far as one hair follicle radius away from the hair duct wall is thermally damaged, with transfer of sufficient heat to prevent hair growth from the follicle for a long period. When the same amount of energy is delivered in a pulse of 100 ms, the temperature rise of the tissue one follicle radius away from the follicle wall is not enough to thermally damage the tissue.

10 However when the fluence is raised from 3 J/cm² to 6 J/cm² for the 100 ms pulse, the temperature rise in the tissue between the wall of a follicle and one follicle radius away from the wall is over 30° C for a period of about 0.1. The corresponding absolute temperature distribution is about 70° C for a period of about 0.1 second, which is high enough to cause thermal damage of the tissue. By these studies it is discovered that when the pulse duration
15 gets longer, the absorbed energy is more uniformly distributed over the tissue. By the time a pulse duration as long as 1 sec is reached, selective thermal damage of the tissue immediately surrounding a hair follicle is almost impossible. Thus, from the point of view of selectively damaging the tissue near a hair follicle, a shorter pulse is preferred. However, as a general rule, the shorter the pulse duration, the greater the danger of causing undesirable destruction
20 of skin.

The invention thus provides improvements in known methods of laser hair removal procedures. It allows the practitioner to control the thermal and/or mechanical damage administered to hair follicles either simultaneously or in sequential phases, by selection of the size of particles in a contaminant infiltrated into hair ducts. The invention provides to the
25 practitioner increased control over the difficult task of forcing chromophore particles into the depths of hair ducts using laser light. The invention also affords the practitioner improved control over the amount of heat that is administered to the tissue in and surrounding the hair follicles during lasing. As a result of these improvements, the risk of unwanted damage to skin tissue is lessened, while the techniques of inhibiting hair growth are improved.

No. 8: A METHOD FOR SUNLIGHT-ASSISTED HAIR REMOVAL

Methods of hair removal are known in which a photochemical is infiltrated into hair ducts and then exposed to light having a wavelength absorbed by the contaminant. Upon illumination, the photochemical produces a chemical species that destroys skin tissue in and around the infiltrated hair ducts. For example, Japanese patent No. 63-249577 discloses methods of hair removal that utilize porphyrin and chlorin derivatives, which release singlet oxygen upon irradiation by a frequency-matched light. However, known methods are time consuming and are generally administered in a salon or clinic, making them expensive.

The present invention overcomes some of the difficulties of the art by utilizing sunlight as the light source in a method for long term inhibition of hair growth. This method of inhibiting hair growth can be practiced without any specialized equipment or skills. In this invention, the photochemical is a prodrug that is activated by sunlight to create a chemical species toxic to cells in and surrounding hair ducts that cause hair growth, but is safe for topical application to the surface of skin. Non-limiting examples of sunlight-activated prodrugs that can be used in the practice of this invention are photophrine II, amino levulenic acid, beta carotene and tetracycline.

The sunlight-activated photochemicals are administered at a relatively high dosage, for example about 2% by weight of a aqueous solution. However, it should be noted that a substantially more dilute concentration (for example, one ten times less concentrated than what is used to cause hair removal) will not cause hair removal, but will cause a slight inflammation in the hair follicles sufficient to stimulate hair growth.

In the method of the invention, the sunlight-activated photochemical is applied to the skin surface in an area in which it is desired to inhibit hair growth. Gentle massage is used to infiltrate a portion of the photochemical into hair ducts in the section of skin treated. Due to the extremely high metabolic rate of hair growth cells, the sunlight activated prodrug is preferentially and rapidly absorbed within hair ducts and into cells and adjacent tissue structures that generate hair growth. Such cells include hair papilla cells, stem cells, keratinocytes, and endothelial blood vessels. Absorption of the photochemical into other, more slowly growing cells, is at a substantially slower rate. In addition, the stratum corneum layer

in skin acts as a protective barrier to prevent significant absorption of the photochemical through the skin surface.

A period of time must be allowed for the photochemical to be absorbed by and concentrated in the target hair growth cells. Generally, a period of about 1 to about 7 hours is sufficient time to allow normal biological processes to assist in absorption of the photochemical in the fast-growing target cells. The rest period for any particular photochemical can be determined empirically by one skilled in the art. After this rest period, the contaminated skin section is exposed to direct sunlight for a period of time sufficient to activate the prodrug, thereby causing damage to the hair growth cells. Generally, the time of exposure will be from about three to about four hours, but may in some cases be as little as 20 minutes.

Therefore, in one embodiment of the invention, the sunlight-activated photochemical is applied to the skin surface before retiring to bed, and the next morning the area of skin so treated is exposed to direct sunlight by taking a sun bath or going to the beach for a period of several hours. By timing the illumination in this manner, the hair-producing cells in the follicle, as well as the tissue immediately surrounding the follicle that feed the hair, are damaged by photochemical activation of the prodrug photosensitizer, but without substantial damage to other tissue.

In another embodiment of the invention, the photochemical is entrapped or encapsulated within microcarrier particles in a formulation suitable for topical administration, such as a formulation of liposomes or coacervate microcapsules. FIGS 21A-E show different types of microcarriers containing a photochemical. As shown in FIG. 22, the microcarrier particles containing the photochemical are applied topically to the skin surface 12 and induced to penetrate into a hair duct 31 in the spaces around hair shaft 33, for example by gentle massage of the skin surface. An ultrasound vibrator 18 may be applied to the skin surface 12 to force the microcarrier particles 20 into the hair duct 31 as shown in FIG. 23.

The lining of hair ducts does not have an epithelial barrier layer, such as the stratum corneum. Consequently, the lipids in lipid-based particles, such as liposomes, enhance penetration of the prodrug across the cell walls of papilla cells, stem cells, and keratinocytes in the infiltrated hair ducts. Then, irradiation of the skin surface with sunlight as described above activates the photochemical prodrug so as to damage these hair growth cells.

To accommodate this function, the microcarrier particles are sized large enough to avoid absorption across the stratum corneum at the skin surface, but small enough for entry and passage into the hair duct. For application to humans, the diameter of the microcarrier particles is generally less than about 70 μm , for example about 10 μm to about 50 μm because the diameter of hair ducts in humans is in the size range from about 70 μm to about 1 micron.

Methods are well known for encapsulating an active agent within a microcarrier particle, such as a liposome or a microcapsule. For example, there are at least three types of liposomes. Multivesicular liposomes (MVL) are man-made, microscopic lipid vesicles comprising lipid membranes enclosing multiple non-concentric aqueous chambers. Multilamellar liposomes or vesicles (MLV) have multiple "onion-skin" concentric membranes, in between which are shell-like concentric aqueous compartments. Multilamellar liposomes and multivesicular liposomes characteristically have length-weighted mean diameters in the micrometer range, usually from 0.5 to 25 μm . Unilamellar liposomes or vesicles (ULV) are liposomal structures having a single aqueous chamber, usually with a mean diameter range from about 20 to 500 nm.

Multilamellar and unilamellar liposomes can be made by several relatively simple methods. The prior art describes a number of techniques for producing ULV and MLV (for example U.S. Patent No. 4,522,803 to Lenk; 4,310,506 to Baldeschweiler; 4,235,871 to Papahadjopoulos; 4,224,179 to Schneider; 4,078,052 to Papahadjopoulos; 4,394,372 to Taylor; 4,308,166 to Marchetti; 4,485,054 to Mezei; and 4,508,703 to Redziniak). Methods for making multivesicular liposomes are disclosed in Kim *et al.*, *Biochem. Biophys. Acta*, 728:339-348, 1983). For a comprehensive review of various methods of ULV and MLV preparation, refer to Szoka, *et al. Ann. Rev. Biophys. Bioeng.* 2:465-508, 1980.

Also contemplated within the scope of this invention is a composition for topical application to a skin surface for inhibiting hair growth on the skin surface. The composition comprises a sunlight-activated prodrug encapsulated in a microcarrier particle, such as a liposome or microsphere. The diameter of the particles is generally less than 70 μm , for example about 10 μm to about 50 μm . In one embodiment, the sunlight activated prodrug is selected from the group consisting of photophrine II, amino levulenic acid, and tetracycline.

The composition further comprises a physiologically acceptable carrier suitable for topical application. The carrier may comprise any conventional topical formulation base, such as those described in Remington's "Pharmaceutical Sciences," 17th Edition (Mack Publishing Co., Pa), the disclosure of which is incorporated by reference. A lotion, suspension in oil, solution, cream, ointment, gel, aerosol, or nebulized formulation are representative of the topical compositions of this invention.

This method for inhibiting the growth of unwanted hair provides the advantage of home treatment because the light source used to activate the photochemical prodrug is sunlight. A topical composition containing the sunlight-activated prodrug can be self-administered, and, after a rest period to allow accumulation of the prodrug in hair-growth cells lining hair ducts, a simple sun bath is all that is required to activate the prodrug and thereby inflict sufficient damage to inhibit hair growth on a long term basis.

No. 9: A METHOD FOR INHIBITING HAIR GROWTH USING ANTI-PROLIFERATIVE AGENTS

It is known to infiltrate photoactivated chemical compounds, such as porphyrin and chlorin derivatives, into hair ducts, and then to illuminate them with light at a wavelength that causes the photochemicals to release species harmful to cells in hair follicles responsible for hair growth. However, the light sources used for illumination, such as lasers, are expensive and usually require trained operators to avoid unwanted damage to skin and eyes.

The present invention provides a method for temporarily inhibiting growth of unwanted hair on a section of skin by topically applying an anti-proliferative agent to the section of skin to be treated. The anti-proliferative agents do not require activation by any type of light source. Normal hair growth will recommence once the treatment is withdrawn.

During application of the anti-proliferative agent, care is taken to assure that at least a portion of the anti-proliferative agent is delivered into hair ducts on the section of skin to be treated to inhibit hair growth. Preferably the anti-proliferative agent is delivered along the full length of the hair duct, which length varies depending upon the bodily location of the skin section to be treated (*i.e.*, on the face, legs, or arms). The depth of the hair duct also varies for an individual hair depending upon the phase of the hair growth cycle in which it is found.

During the mature anagen phase, for example anagen V and VI, the hair follicle is fully extended (to a depth of 3.0 to about 5.0 mm), and the distance to the bottom of the follicle from the skin surface is about twice that during the telogen phase of the hair growth cycle. Therefore it is advantageous to synchronize the growth cycle of the hairs to be treated before
5 application of the anti-proliferative agent to the area to be treated for inhibition of hair growth. Methods for synchronizing the hair growth cycle are disclosed above in Section No. 1 herein.

The anti-proliferative agent is applied to the skin surface in any suitable topical formulation, such as a lotion, cream or gel. Suitable formulations preferably are designed to
10 aid in delivery of the anti-proliferative agent into hair ducts, and may therefore, include one or more chemical agents that will reduce surface tension, such as a surfactant.

Anti-proliferative agents useful in the practice of this invention include small molecules as well as macromolecules, such as proteins or enzymes, that interfere with or interrupt in any way the cycle of cell proliferation. Representative examples of anti-prolifera-
15 tive agents useful in the compositions and methods of the present invention include methotrexate, doxorubicin, taxol, tumor necrosis factor, chlorambucil, interleukins, etoposide, cytarabine, fluorouracil, vinblastine. The mechanism of action of the anti-proliferative agent is immaterial other than that it interferes with or interrupts the cycle of cell proliferation. For example, methotrexate, aminopterin and cytosine arabinoside (also known as
20 cytarabine and Ara-C) are cell cycle-specific antimetabolites that kill cells only when they are synthesizing DNA. Fluorouracil inhibits formation of both DNA and RNA. Methioninease is an enzyme that inhibits uptake of methionine by hair papilla cells proliferating at a high rate.

Hair ducts are not lined by an epithelial barrier layer, such as the stratum corneum, but do contain rapidly proliferating hair papilla cells, stem cells, keratinocytes, and endothe-
25 lial blood vessels, which generate hair growth. These cells in the hair duct responsible for hair growth are the fastest growing cells in the body, aside from tumor cells. Due to the absence of a barrier layer in the hair duct, the anti-proliferative agents are preferentially taken up by these hair growth cells, which have a high metabolic rate. Entry of the anti-proliferative agents into other, more slowly growing cells, is at a substantially slower rate. Conse-

quently, the anti-proliferative agents are preferentially absorbed into the target hair growth cells, with the result that hair growth is inhibited.

Application of the anti-proliferative agent to the skin surface is repeated at spaced intervals of hours or days until hair growth is inhibited. Generally, the anti-proliferative agent is applied two times daily for so long as it is desired to inhibit the growth of hairs from the treated portion of the skin. Once treatment is stopped, hairs in the treated section of skin will commence a normal growth pattern.

In one embodiment, the anti-proliferative agents are encapsulated in lipid-based particles, such as liposomes or microcapsules, for application to the skin surface. The lipid-based particles are sized small enough to enter into hair ducts in the section of skin, but large enough not to be absorbed across the stratum corneum. Care is taken during application of the lipid-based particles to assure that at least a portion of the drug-bearing particles enters into the hair ducts. For example, the micro particles can be formulated in a physiologically acceptable carrier containing one or more chemical agents that will aid entry of the particles into hair ducts. It is believed that administration of the anti-proliferative agents encapsulated in lipid-based particles will increase uptake of the anti-proliferative agent. As the lipid-based particles begin to break down in the hair duct, both the encapsulated drug and lipids from the bilayers of the lipid-based particles are released. These lipid byproducts can aid in delivery of the released drug across the cell membranes of the target cells. Methods for obtaining an active agent encapsulated in lipid particles, such as liposomes and microcapsules are well known in the art and are referred to above in Section No. 8 herein.

Lipid-based particles, such as liposomes, deliver the encapsulated agent slowly within the hair duct, so that the cells lining the hair duct are bathed in the anti-proliferative agent over an extended period of time, generally over a period of hours or even days. Slow release of the anti-proliferative agent from the lipid-based particles is particularly advantageous for those agents that interfere with a particular step in the proliferation cycle of the cells, such as formation of DNA and/or RNA, because not all cells enter mitosis at the same time.

The dose of the anti-proliferative agent administered, whether encapsulated or unencapsulated, can vary from about a few picomoles to about several hundred millimoles. The desirable dose of anti-proliferative agent per unit area of skin treated is a hair growth-

inhibiting amount, and will vary depending upon such characteristics as the stage of target hairs in the hair growth cycle at the time of administration, the age and condition of the subject, the particular properties of the agent, and the dosage schedule. In general, the dosage range of the anti-proliferative agent appropriate for topical application to humans is in the range of about 0.001 to about 6,000 mg/m² of body surface area, generally applied in a cream, ointment or solution containing about 10% of the anti-proliferative agent by weight. While doses outside the foregoing dose range may be given, this range encompasses the breadth of use for most anti-proliferative agents useful for inhibiting hair growth. The dose range for a particular anti-proliferative agent can be easily ascertained as previously described.

The present invention provides the advantage over other hair removal procedures that no specialized equipment is required to inhibit growth of unwanted hair. No lasers, razors, depilatory needles, *etc.*, are required for safe and temporary inhibition of hair growth. The anti-proliferative agent is repeatedly applied onto the surface of skin so as to cause the anti-proliferative agent to enter hair ducts therein, and hair growth will recommence upon cessation of the treatment. The embodiment of the invention in which the anti-proliferative agent is administered in a slow release lipid-based formulation provides convenience by reducing the number of times the formulation must be used to accomplish the goal of inhibiting hair growth.

No. 10: USE OF METHIONINE TO STIMULATE HAIR GROWTH OR REGROWTH

Among many people, there is great interest in stimulating the growth or regrowth of human hair. For example, alopecia, especially male pattern baldness, is a condition that is common to a large proportion of the male population. The present invention provides a method for stimulating hair growth or regrowth to reduce the symptoms of hair loss.

It is known that the amino acid methionine is required by the body for rapid cell proliferation, such as in the growth of tumors. The inventors herein have discovered that application of methionine to a skin section so that it penetrates into the hair ducts to contact hair growth cells therein can be used to induce growth of hairs from follicles therein. (The

anagen stages of the hair growth cycle are characterized by rapid proliferation of hair growth cells). In some cases, even if growth of hairs from the target follicles has ceased for a considerable period of time, the administration of methionine into the hair ducts, so as to contact the hair growth cells, *i.e.*, the hair stem cells, will restore hair growth. In other cases, vellum hairs have been restored to normal pigmented hair growth by the application of methionine to the hair growth cells in hair ducts.

Methionine is administered to hair growth cells in a hair follicle in a hair growth stimulating amount, which may differ depending upon the phase in the hair growth cycle, the anatomical location of the hairs, such factors as the age and general health of the patient, and the dosage schedule. Taking these factors into account, one of skill in the art will be able to determine the appropriate timing and amount of doses appropriate for any individual in need of treatment. In general, however, it is recommended that a dose of about 0.001 to about 6,000 mg per square meter of skin surface to be treated should be rubbed into the skin section twice a day, for instance morning and night. As methionine is non-toxic to all mammals, there is no known overdose effect.

The treatment should be continued until satisfactory hair growth has been restored. In some individuals restored or enhanced hair growth is noticed in as little as about 3 to about 5 weeks, while in others a noticeable difference in hair growth or regrowth is not noticed until the treatment has been continued for a period of several months, for example, 5 months.

To enhance penetration of methionine into hair ducts and enhance uptake of the amino acid by hair growth cells therein, the methionine can be administered in a liposome or other lipid-based microparticle. The properties of liposomes and methods for encapsulating a biologically active agent, such as methionine, into liposomes are described in Section No. 8 herein. The methionine can also be contained in a formulation suitable for topical administration, such as an ointment, cream, suspension or solution.

The present method of stimulating hair growth by contacting hair growth cells with sufficient methionine to stimulate hair growth cells in hair ducts has an advantage over prior art hair stimulation compounds and methods of their use in that methionine is not toxic to mammals. In addition, as it is an amino acid, Methionine is inexpensive to use in comparison with prior art hair growth stimulating drugs, such as Minoxidil.

No. 11: A METHOD FOR TREATING HERPES WITH LASER

Seroepidemiologic studies have shown that infections of Herpes viruses are found worldwide. Infections of Herpes Simplex (oral or genital) or Herpes Zoster virus can manifest as skin lesions and/or rash at almost any location on the body. After a primary
5 infection subsides, Herpes virus is reported to reside within the skin at the bulge area of the hair duct during latent phases of the disease. For this reason, mild trauma to the skin, or any treatment of the skin with a topical medication or lotion, can be followed by reactivation of the disease. It is known to treat such manifestations with an anti-viral agent that interferes with the replication of viral DNA, for example, oral administration of acyclovir or a topical
10 5% acyclovir ointment or cream.

The present invention provides an alternative method for preventing Herpes outbreaks on the skin of susceptible individuals and/or treating infections of Herpes viruses on skin. During latency, Herpes viruses reside in the bulge area of the hair follicles. FIG. 1 shows a cross-section of a hair duct with a hair shaft 33, sebaceous gland 38, and bulge area 40. The
15 hair growing in the hair duct shown in FIG. 1 is in the anagen phase of the hair cycle, so that the follicle is extended to its full length, and the bulge area 40 of the hair duct is located about one-half way down the follicle, just below the sebaceous gland.

In this invention, reactivation of a Herpes virus infection in the form of skin lesions is prevented or treated. To prevent reactivation, hair ducts in the infected skin section are
20 infiltrated with a light-absorbing contaminant so that at least a portion of the contaminant enters the bulge area of hair ducts containing latent Herpes viruses. Then the contaminated skin section is illuminated with short pulses of light at a wavelength more highly absorbed by the contaminant than by skin. Light energy absorbed in the form of heat or kinetic energy by the infiltrated contaminant in and around the bulge area is transferred to the latent viruses
25 residing in the hair ducts. As a result, the Herpes viruses are denatured or destroyed, rather than suppressed in replication. By taking these steps, an outbreak of a Herpes skin infection is prevented.

A Herpes skin infection can also be treated during an episode of reactivation using the method of this invention. During a reactivation of a Herpes skin infection, latent viral
30 particles in hair ducts become active and multiply, with transmission of viral particles up

through the hair duct to the skin surface. By practice of this invention during an episode of reactivation, viral particles throughout the hair duct are heated and destroyed.

The methods of this invention are variations of laser hair removal techniques. It has now been discovered that these methods can be used to destroy or eradicate Herpes viruses sequestered within hair ducts in an infected skin section, whether or not the hair ducts contain viable hairs. U.S. Patent Nos. 5,226,907 and 5,425,728 to Tankovich, which are incorporated herein in their entireties, disclose methods for hair removal and/or long term inhibition of hair growth utilizing a light absorbing contaminant that is infiltrated into hair ducts and then illuminated with short pulses of light. The contaminant is generally a water or oil-based suspension or solution containing chromophore particles having a good absorption at or near at least one frequency band of light, but any type of contaminant that absorbs light energy can be used. If the contaminant contains chromophore particles, for example carbon or graphite particles, they are generally sized too large to penetrate the barrier layer of the stratum corneum, but small enough to readily infiltrate the treated hair follicles. These techniques are modified in the present invention in that hair ducts containing latent viruses are infiltrated with the contaminant so that at least a portion of the contaminant enters the bulge area of the hair ducts adjacent to the latent viruses. Then the contaminated hair ducts are illuminated with short pulses of a light beam containing at least one wavelength that is well absorbed by the contaminant, but which penetrates skin with a minimum of absorption and scattering therein, such as that produced by a Nd:YAG laser. The short pulses of light can be used to cause explosions in the particles so as to drive the contaminant deep into the bulge area of hair follicles. The short pulses of light also cause heating of the contaminant.

Heat generated in irradiated contaminant in and around the bulge area of hair ducts is transferred to viral particles either by conduction or by transfer of kinetic energy from explosion of particles in the contaminant. The short pulses of light may also destroy viral particles on a skin surface if the viral particles absorb the frequency of light used during the illumination, or if there is sufficient contaminant on the skin surface to absorb heat from the pulses of light. Generally, to destroy viruses in hair ducts, *i.e.*, in the bulge area, the viral particles contained therein should be raised to a temperature of about 70°C to about 80° C for about 0.1 to 1.0 second. The size and material of the light absorbing chromophore particles in

the contaminant should be matched to the properties of the light source so as to deliver sufficient heat to the bulge area of the infected skin section to provide the necessary heat to destroy the viral particles without substantial damage to the skin section treated. In general, the particles are sized large enough to avoid penetration of the particles through the stratum corneum, but small enough to enter into the opening of hair ducts. As the diameter of hair ducts in humans is generally in the range from about 70 μm to about 1 micron in size, the particles are generally in the range from about 0.01 micron to about 1 micron.

To avoid overheating of surface skin tissue, the light source should be absorbed by the contaminant, but should penetrate skin with a minimum of absorption and scattering therein. If a laser is the light source, any of the lasers useful in treatments to inhibit hair growth by infiltrating a contaminant into hair ducts can also be used in the practice of this invention. In one embodiment, the contaminant contains carbon particles, and the light source is a Nd:YAG laser providing short pulses of light having the following properties:

Wavelength	about 1064 nm
Beam Shape:	circle or square
Beam Size:	about 8 mm (circular) of 7x7 mm (square)
Fluence	1-2 J/cm ²
Pulse energy	0.5 J/pulse

The clinical manifestations and course of a Herpes episode depend on the anatomic site of the infection, the age and immune status of the host, and the antigenic type of the virus, *i.e.*, whether HSV-1 or HSV-2. The spread of virus to the skin from peripheral sensory nerves helps explain the large surface area that may be affected, and the high frequency of new lesions distant from the initial crop of vesicles.

Individuals who are particularly susceptible to Herpes infections in skin are those who are immunocompromised and those who manifest other types of skin conditions indicative of immunocompromise. For example, individuals with psoriasis, Darier's disease, eczema herpeticum, or atopic eczema are thought to be susceptible to cutaneous HSV infections due to reduced numbers of circulating NK cells and a decrease in IL-2 receptors in the diseased tissue (H. M. Goodyear, *Br. J. Dermatol.* 134: 85-93, 1996). In such individuals, the method of this invention is particularly useful either prophylactically to prevent reactivation of the virus in skin lesions, or as a treatment of an existing viral activation or reactivation.

The mechanisms by which various stimuli cause reactivation of HSV infection are not known. Ultraviolet light, immunosuppression, and trauma to the skin or ganglia are associated with reactivation. Some hair removal techniques that cause trauma to the skin, such as waxing, use of contaminants in hair ducts, or use of chemical depilatories, may trigger an outbreak of Herpes in the skin section involved. The method of this invention is also effective for treating skin to prevent such outbreaks or eradicate Herpes virus throughout hair ducts when a manifestation of a viral infection has been triggered by hair removal techniques that cause trauma to the skin, even if the hair ducts involved no longer contain hairs.

By the methods of this invention, Herpes outbreaks on skin can either be prevented or treated without reliance upon systemic administration or topical application of an anti-viral agent. Thus, patients with low tolerance for such agents, or who choose to avoid exposure to drugs, can be treated using a relatively inert contaminant, *e.g.*, carbon particles and light.

No. 12: A METHOD FOR REDUCTION OF SWEAT AND BODY ODOR

Human bodies produce sweat to reduce overheating and in response to emotional stimulæ. Sweat is produced by glands (sudorific or sweat glands) situated at a depth of about 1 to 2 mm below the surface of the skin on almost all of the body surface. Bacterial action causes decay of proteinaceous compounds in sweat, creating undesirable body odors. Prior art methods for reducing production of sweat and/or treating body odor include various creams, gels and powders that block production of sweat or combat growth of bacteria.

Laser treatment can be used to reduce human odor and/or the production of sweat. In this invention, known laser hair removal methods are modified for use in inhibiting production of sweat from sweat glands.

Sweat glands are distributed widely over the surface of the skin and are found in almost all locations of the body. In the present invention, a section of skin containing sweat glands is infiltrated with a contaminant, for example one containing carbon particles. The particles are infiltrated into spaces in or adjacent to sweat glands via hair ducts. Then the skin surface is illuminated with short pulses of laser light that is preferentially absorbed in the particles, but is minimally absorbed in skin. As the blood vessels that supply blood to sweat glands are located at a depth of about 1 to about 2 mm below the surface of the skin, during

illumination of the skin surface with the short pulses of light, a lens with a short focal length is used to focus the light at a depth of about 1 to about 2 mm below the skin surface to destroy the sweat glands. In one embodiment, a light with a wavelength in the range from about 532nm to about 600 nm is used to destroy blood vessels supplying blood to sweat glands. Once the skin surface has been illuminated so as to denature the sweat glands and/or the blood vessels feeding the sweat glands, the production of sweat and/or body odor in the section of skin so treated is reduced or eliminated.

Alternatively, production of sweat can be inhibited by orally administering sodium fluorescein to a subject, waiting for the sodium fluorescein to accumulate in sweat glands, and then illuminating a skin section in which inhibition of sweat is desired with light having a wavelength that is well absorbed by the contaminant sodium fluorescein, but is not well absorbed in skin tissue.. Sodium fluorescein is a biocompatible photosensitizer, and when administered orally is preferentially delivered to sweat glands by metabolic processes within about one hour in sufficient concentration to serve as a light-absorbing chromophore.

Metabolic processes will eventually deliver the photosensitizer to other skin tissue, so it is important to time the illumination of skin tissue for destruction of sweat glands during the window of time when a tissue destroying amount of the photosensitizer has accumulated in the sweat glands, but before a tissue destroying amount of the photosensitizer has accumulated generally in skin tissue.

A tissue-destroying amount of a solution of disodium fluorescein generally contains a concentration of about 2% to about 10% by weight, with the total amount varying depending on such factors as the weight and metabolism of the subject.

Although any light can be used that produces a wavelength of about 441 nm, a preferred light source is a He:Cd laser or a Nd:YAG doubled frequency laser. Upon activation by light at a wavelength of about 441 nm, sodium fluorescein emits energy in the form of a green light that is well absorbed by blood in capillaries that feed the sweat glands, causing the chromophores in the blood to become heated. By this means of energy transfer, the blood in the capillaries is heated sufficiently to damage the blood supply to the sweat glands, *e.g.*, by coagulation of the capillaries. Thus, the blood supply to the sweat glands is

cut off or diminished sufficiently to cause the sweat glands to wither, inhibiting production of sweat and consequent odor.

The methods for reducing human sweat and body odor of this invention offer the advantage that inhibition of sweat production is long term; whereas prior art methods in which a cream or ointment is applied to skin inhibit sweat production only for a few hours, at most.

No. 13: TAILORED LASER ASSISTED HAIR REMOVAL

Current methods of laser assisted hair removal utilize a set of laser parameters that are selected to fit the absorption characteristics of a particular exogenous chromophore applied to the hair ducts or a particular naturally occurring chromophore, such as water, blood or melanin. If the laser parameters are adjusted at all to fit individual patients, they are commonly adjusted by hand to accommodate such factors as individual differences in skin or hair coloring, differences in follicle depth at different anatomical locations, and the like. It would be advantageous to have a more systematic method for optimizing laser parameters to fit individual requirements, or an automated system whereby upon input of information regarding an individual's coloring, *etc.*, the system would set a laser apparatus to provide optimal laser parameters corresponding to the input information.

A method is provided for tailoring laser-assisted hair removal to the needs of an individual patient. The treatment regimen and selection of treatment parameters is based on consideration of answers to a set of predetermined questions regarding various aspects of a patient's characteristics and treatment history that will affect selection of laser parameters and scheduling of treatments. The set of questions should comprise at least the following: (a) what is the patient's skin coloration, *e.g.*, whether dark or fair; (b) what is the anatomic site of treatment, and what is the average depth of hair follicles at the site; (c) what is the current status of the hair growth cycle for the preponderance of hairs at the site; (4) what is the individual hair physiology of the patient at the treatment site, *e.g.*, the diameter of the hairs or whether the hairs are vellum; and (5) what previous laser treatment for hair removal has the patient undergone.

In one embodiment of the invention, a system is provided for pre-programming a laser to select optimal laser parameters based on input to the system by an operator regarding the answers to these questions, which are specific to an individual patient. However, the same result can be accomplished by the operator manually adjusting the laser parameters that
5 control the energy level produced by the laser in accordance with the answers to the above set of questions provided by the individual to be treated.

The optimal laser characteristic in terms of wavelength, fluence, pulse repetition rate, and pulse duration generally will vary depending upon the hair coloration of the individual undergoing treatment as well as skin color, extent of sunburn, *etc.* Dark hair, for example,
10 may be more susceptible to a Nd:YAG laser at a wavelength of 532 nm compared to light hair, which is more susceptible to a wavelength of 1064 nm. In general, dark hair absorbs light energy more readily at any wavelength, so less laser energy is needed in treatment of dark hair than in treatment of light colored hair.

The optimal laser characteristics for specific anatomic sites also differ due to
15 differences in the average depth of hair follicles at various anatomical sites. For example, the energy levels utilized in the upper lip region may be less due to the shorter depth of the follicles (1.8 mm) compared to the lower leg region where the follicles may extend to 4.0 mm deep. As described in detail in Section No. 1, herein, the depth of an individual hair follicle also varies depending upon its current phase in the hair growth cycle. In general, the bottom
20 of a hair follicle is at a depth in the range from about 1 mm to about 2 mm during the telogen phase of the hair growth cycle; whereas the bottom of the hair follicle is at a depth of about 4 mm to about 6 mm during the anagen phase of the hair growth cycle. Although, in some cases it may be desirable to omit consideration of the hair growth cycle completely in determining the average depth of hairs at the anatomic site to be treated, if it is to be
25 considered at all, the phase in the hair growth cycle of a preponderance of hairs at the anatomic site generally will be considered together with the location of the anatomic site in determining the average depth of hair follicles at the site to be lased.

It is preferred that the hairs in the section of skin to be treated will be synchronized in a common phase of the hair growth cycle, for example, the late telogen/early anagen phase,
30 prior to lasing for hair removal, as disclosed in Section No. 1 herein. Assessment of the hair

growth cycle for an individual may include a direct measurement of the extent of anagen versus catagen hair. This can be done by shaving or cutting the hair from a specific anatomic area and counting the hairs which are present. After one to eight weeks, the hairs in the same area are recounted using the same procedure. The difference between the initial count and the second count gives the number of hairs which are in anagen. Further description of procedures for assessing the current phase of the hair growth cycle in a section of skin and for synchronizing hairs in the hair growth cycle is in Section No. 1 herein.

The hair physiology of the patient will also influence the selection of laser parameters. For instance, if the patient has undergone previous laser treatment for hair removal, the hairs at the site to be treated may already have undergone a substantial weakening in their general vitality, which is generally characterized by a decrease in diameter and less deeply colored appearance. Another factor relating to hair physiology that may influence the selection of laser parameters or treatment regimen is the patient's nutritional status or disease state. For example, use of steroids or biotin deficiency, which cause temporary hair loss, generally indicate that treatments for hair removal should be delayed until normal health has been restored.

The scheduling of hair removal treatments, *i.e.*, the treatment regimen, is also an important aspect of tailoring the hair removal treatment to the individual patient. In particular, the spacing between hair removal treatments should be closely coordinated with the patient's individual response to the previous treatment. For some patients, hairs do not fall out at a treatment site for about 2 to 3 weeks following a laser hair removal treatment, while for other patients the hairs at a treatment site do not fall out for about 6 or 7 weeks following a laser hair removal treatment. Therefore, if the patient has previously undergone laser hair removal treatment, the treatment site should be closely monitored to detect the loss of hair attributable to the laser treatment. New hairs will emerge from the hair ducts in the treatment site within about 2 to 3 weeks following hair loss. Therefore, a subsequent treatment should be scheduled to take place within about 2 to 3 weeks following hair loss due to a previous hair removal treatment and when less than about 30% of the hairs at the former treatment site are visible above the skin surface in regrowth. If this pattern is followed, hair regrowth will be effectively curtailed at the treatment site.

The spacing of hair treatments is also affected somewhat by seasonal and circadian rhythms in light. For example, in the Northern hemisphere, the largest percent of hairs in telogen phase occurs in the months of August and September, with onset of an increase in the percentage of hairs in anagen phase occurring about three months thereafter.

5 The treatment regimen and the laser parameters for use in hair removal treatments are selected based upon the information obtained by answering the full set of questions, except that any question is omitted that does not apply to a particular individual in the judgment of a skilled operator. This process ensures that all relevant factors are properly evaluated and weighed against one another in selecting the spacing between hair removal treatments and the
10 wavelength of light, fluence, pulse repetition rate, and pulse duration to optimize any type of laser hair removal technique.

In one embodiment, the laser energy, *i.e.*, combination of the wavelength, fluence, pulse repetition rate, and pulse duration of the laser, is selected to deliver a fluence of about 1.5 to about 5 J/cm², for example about 2.5 J/cm², at a depth corresponding to the depth of the
15 majority of the hair follicles in the skin section to be treated, with the wavelength being selected based upon the individual's hair and/or skin color, as described above.

As discussed above, the depth to which the energy must penetrate to damage hair follicles will differ depending upon the predominant phase of the hair growth cycle. In addition, hair follicles in the anagen phase are more susceptible to damage by lasing than at
20 any other phase of the hair growth cycle. Therefore, the optimal laser parameters utilized in treating a site predominantly in anagen phase will include a lower laser energy than is required for a site predominantly in telogen phase.

For example, treatment of each patient may be tailored by performing the following series of steps with regard to an individual patient. For some patients it will be apparent that
25 not all of the steps will be appropriate, in which case an inappropriate step is omitted, and the operator passes to the next step in the series. However, it is important for the operator to at least consider whether each step is appropriate for each individual to be treated.

In one embodiment the series of questions to be considered in determining the optimal laser parameters comprises the following:

- Does the patient exhibit any symptoms, such as a skin rash or bad sunburn, that are contraindications for laser hair removal? If yes, terminate the treatment and reschedule at a later date. Contraindications include, but are not limited to, existing pregnancy; a history of metastatic skin tumors, such as basal cell, squamous cell, or melanoma; an HIV positive condition; or a mole containing a hair growing in the treatment area.
- Has the patient undergone a previous treatment for hair removal? If yes, schedule the next treatment to occur when hair regrowth is visible from about 30% of the hair ducts at the previously lased site.
- What is the color of the patient's hair and skin at the anatomic site to be treated? Where is the anatomic site to be treated? Preferably the anatomic site to be treated will be photographed to document hair and skin coloration. Select a wavelength of light to be used based on skin color and hair color.
- Optional: What is the predominant phase in the hair growth cycle of hairs in the site to be treated? It may be desirable to avoid this question to save the costs involved with obtaining an answer to this question.
- The site may optionally be pretreated to synchronize the growth of hairs in the hair growth cycle to fix the average depth of the hair ducts (or follicle) at a common depth at the anatomical site. Preferably the hairs are synchronized in the late telogen/early anagen phase.
- Select optimum laser operating characteristics, such as wavelength, fluence and pulse duration based on the foregoing information. The correlation between patient characteristics and laser parameters is empirically determined.
- Initiate laser injury of the follicles to induce hair growth inhibition.

One of skill in the art will be able to determine whether additional questions need to be answered in arriving at a set of laser parameters that are tailored to an individual patient.

This invention provides the advantage that the laser parameters used in treatments to inhibit hair growth and the treatment regimen are tailored to fit individual characteristics of

the patient, rather than using a fixed set of parameters for all individuals that is selected to fit the absorption characteristics of a particular exogenous or endogenous chromophore to be irradiated. In addition, as shown in FIG. 24, the method can be used in connection with a computerized system 72 in communication with a laser 74 so that the laser operator can key in responses to a set of predetermined questions regarding the patient's hair, skin, physical condition, and anatomical location to be lasered with the result that a preprogramed selection of individually tailored laser parameters is transmitted to the laser before lasing is initiated.

No. 14: IMPROVED LASER OPERATING CHARACTERISTICS FOR HAIR FOLLICLE DAMAGE

A number of methods are known for using lasers to inhibit hair growth and/or cause damage to hair follicles in a section of skin, including a method for infiltrating into hair ducts a contaminant containing carbon particles suspended in an oil, and irradiating the section of skin with pulses of laser light.

The optimal laser operating characteristics have now been discovered for inducing targeted hair follicle damage when a contaminant containing carbon particles suspended in a liquid, such as an oil, is infiltrated into hair ducts, and the section of skin containing the hair ducts is irradiated with pulses of laser light. These improved parameters are as follows:

Laser Type:	Nd:YAG
Wavelength	1064 nm
Beam Shape:	Circle or Square
Beam Size:	≤ 8.0 mm
Fluence:	> 2 J/cm ²
Pulse Duration:	Depends upon many factors, including:

1. The size of carbon particles or other chromophores in the contaminant.
2. The concentration of the chromophore in the lotion or solution applied to the skin prior to lasing.
3. The depth of hair follicle (which is dependent on the anatomical site and the phase in the hair growth cycle).
4. The thermal properties of the chromophore.

The effect of pulse duration on heating and/or explosion of chromophore particles is described in full detail in Section 4 herein.

For a 10 ns pulse of about 2 to about 3 J/cm² fluence, a carbon particle size much less than 1 micron is needed for the photothermal effect to be greater than the photomechanical effect. Longer pulse durations are preferred with larger particles. However, when larger particles are used, surface cooling of the skin, for example, as disclosed herein in Sections 3 and 20, may be needed to avoid over heating and damage to surrounding skin.

No. 16: *IN SITU* FORMATION OF A PHOTORECEPTOR FOR USE IN LASER HAIR REMOVAL OR SKIN REJUVENATION TREATMENTS

Widespread use of lasers to remove tattoos has demonstrated that residual carbon in skin structures is not permanent. However, the mechanism used by the human body to clear residual carbon particles introduced into hair follicles and other skin structures during treatments for laser hair removal or skin rejuvenation is an open question. Additional exogenous chromophores useful in performing laser hair removal or skin rejuvenation treatments would be desirable.

It is known that elemental iron is readily taken up by the body and used to replenish the approximately 1 mg of the element that is lost daily from shedding of senescent cells along the gastrointestinal and genitourinary tracts, and from desquamation of skin. This minimum daily requirement is increased by growth spurts, pregnancy, and pathologic hemorrhage (*Harrison's Principles of Internal Medicine*, 13th Edition, Ed. Isselbacher *et al.*,

Vol. 2, 1994, page 1722). Because of these factors, iron oxide has been safely applied to human skin and hair in cosmetics for centuries. Iron oxide is also an especially safe exogenous chromophore for use in any of the hair removal or skin treatments wherein an exogenous chromophore applied to the skin is irradiated, as it is highly unlikely that harmful effects would result from any iron that might remain in hair ducts or embedded in the layers of the stratum corneum. Other benign metals that can be substituted for iron in the practice of this invention are those, such as cobalt and copper, for which the human body has a dietary requirement.

Iron oxide and the oxides of other benign metals can be easily formed within hair ducts or within other structures of the stratum corneum that have an opening to the skin surface. For example, iron oxide in the form of limonite, the trihydrate of ferric oxide, is readily formed by applying to skin a solution of ferric chloride *e.g.*, in water. Upon application to skin, and within such skin structures such as hair ducts and sebaceous glands, a double replacement reaction with natural electrolytes in or on skin surfaces forms ferric oxide trihydrate.

Iron oxide absorbs one or more wavelengths of light produced by infrared lasers. For example, limonite broadly absorbs light having a wavelength from about 0.1 micron to several microns, as do many inorganic compounds, which generally lack the sharp absorption bands characteristic of organic molecules. Thus, such inorganic compounds are useful for visible light lasers as well. Limonite appears brownish orange in color in part because it absorbs green light.

The technique for loading spaces in hair ducts or surface layers of the stratum corneum with an oxide of a benign metal formed *in situ* is illustrated with respect to iron, but one skilled in the art can readily adapt the procedure for *in situ* formation of alternative metal oxides that absorb light at a frequency not readily absorbed in skin, for example in the infrared range. First, a skin section to be treated is coated with a water-based lotion or suspension comprising the metal species as a chloride. For iron, the lotion or suspension comprises an acid iron salt solution, such as ferric ammonium sulfate, ferric citrate or ferric chloride in water, with ferric ammonium sulfate being less harsh to the skin than the strongly acid chloride. The water-based suspension or solution optionally further comprises a suitable

nonionic surfactant, such as Tween 20™ (polyoxyethylene sorbitan monolaurate), or any other mildly detergent compound, to overcome surface tension and thereby facilitate transport, *i.e.*, “wicking,” of the ferric compound into hair ducts. Examples of suitable surfactants for use in the invention include, but are not limited to, polyoxyethylene sorbitan monolaurate, Tween® 20-50, sodium laurel sulfate, and lauric acid.

The lotion is applied to the skin surface and allowed to stand for a few minutes, for example about 5 to about 20 minutes. During this rest period, at least a portion of the ferric salt in the lotion or suspension is transformed to ferric oxide trihydrate within hair ducts, within sebaceous glands, as well as in and around loose cells on the surface of the skin.

However, the metal salts can be irritating in high concentrations or after long exposures. To avoid irritation, the metal salt can be wiped from the surface of the skin, and, rather than waiting for the oxide to develop by exposure to natural electrolytes in skin, the iron oxide is formed *in situ* by application to the skin of a basic solution, such as ammonia water or sodium bicarbonate.

An exogenous chromophore produced *in situ* will behave similarly to prior art exogenous chromophores in hair removal and skin rejuvenation techniques. For example, such a chromophore will absorb light energy in the form of heat, which is then released by conduction to adjacent tissue, whether the chromophore is on the surface of the skin or deep within hair ducts. Accordingly, when surface skin cells are to be removed to accomplish a “peel” for the purposes of skin rejuvenation, the metal chloride is applied to the section of skin to be treated so that it infiltrates the topmost few layers of skin cells in the epidermis, and is allowed a period of time for the light-absorbing chromophore to spontaneously form. Finally the section of skin is illuminated with a light beam that is well absorbed by the exogenous chromophore, but which passes through skin with minimal absorption. In this case, the section of skin is generally not cleaned or wiped beyond the removal of grossly excessive quantities of the applied material or the *in situ* formed chromophore before application of the light beam.

However, when the *in situ*-formed chromophore is to be illuminated within skin structures, the *in situ*-formed chromophore is generally cleaned from the skin surface prior to application of the light beam. A formulation containing a sufficient amount of a chelating

agent for ferric oxide to sequester the chromophore is used for this purpose. For example, a solution of citric acid or ethylene diamine tetraacetic acid tetrasodium salt will chelate iron oxide. The chelated chromophore can be cleaned from the skin, for example, with a clear water rinse, prior to illumination of the area to be treated. Upon illumination of the cleaned skin surface with a light beam having at least one wavelength of light well absorbed by the chromophore in the hair ducts, sufficient heat can be generated to cause long term inhibition of hair growth, using any of the known methods described in the Tankovich patents incorporated by reference herein.

For use in hair removal, formation of the exogenous chromophore within hair ducts of a section of skin to be treated for hair removal eliminates the need to mechanically force the exogenous chromophore into hair ducts by massage, explosion of confined particles, *etc.* In addition, since humans have a known daily requirement for certain metals such as iron and zinc, there is minimal risk of residual chromophore causing a problem to an individual treated by the method of this invention.

No. 17: METHODS FOR IMPROVING A HAIR REMOVAL PROCESS

Under magnification, an apparently smooth skin surface is revealed as an uneven terrain with fissures, holes, indentations or irregularities. The indentations may contain minute particles of lint, dead cells, *etc.* These imperfections in the skin surface result in scattering of incident light. In addition, due to the change in the index of refraction between air and skin, photons in a light beam incident on skin, such as provided by a laser, tend to be reflected, refracted or scattered. As a result, a large portion of the light energy directed to a skin surface is lost. FIG. 25A shows a cross-section of a skin surface 12 with incident light beam A partially reflected in beam B and partially refracted in beam C.

In this invention a method is provided for reducing light loss by scattering and reflection at a skin surface during skin lasing techniques. To reduce light loss, the skin surface is covered with a liquid coating or device, *i.e.*, a window, that is transparent to incident light. The covering presents a smooth upper surface to incident light, and is made of a material having a refractive index slightly greater than, or equal to, the index of refraction for skin.

It has been discovered by the inventors herein that loss of light incident upon a skin surface, for example during skin lasing techniques, can be reduced by covering the skin surface with a cover having a smooth surface. The covering can be provided by any material, either liquid or solid, that can rest atop a skin surface to be illuminated, but which will present a smooth surface to receive an incident light beam and transmit the beam without substantial attenuation to the skin surface beneath the covering. To accomplish this without substantial loss of light energy, the covering is substantially transparent to incident light, and has a refractive index slightly greater than or about equal to the index of refraction of skin, which is about 1.37. In use, the covering is placed atop the skin surface to be illuminated so that the incident light strikes the smooth surface and is transmitted to the skin through the covering.

In one embodiment shown in FIG. 25C, the covering is a contact plate 44 having at least one smooth planar surface 46, such as a thin plate of an inert and substantially transparent material. In use, the contact plate 44 rests atop a skin surface 12. Transparent plastic, glass, quartz, fused silica, or a polymeric material can be used to make the contact plate 44. Table 5 below shows the index of refraction for representative materials that can be used for the contact plate.

Table 5

Material	Index of Re- fract
Corning glass 7913	1.45 @ 1.0 μ m
Glass (Bk-7)	1.51 @ 1.0 μ m
Quartz	1.53 @ 1.0 μ m
Fused silica	1.45 @ 1.0 μ m
Styrene/vinyl benzene	1.55 approx.
Skin	1.37 approx.
Mineral oil	1.47 approx.

An antireflective coating (not shown) on the side of the covering that faces the laser (*i.e.*, planar surface 46) will minimize loss of light energy during transfer all the way through to the skin. The contact plate may take a variety of shapes. For example, the shape of the contact plate may be circular, trapezoidal, square, *etc.* The skin surface to be irradiated may be somewhat concave or convex, depending upon its anatomical location. Therefore, for convenience in use, the surface area of the contact plate that contacts a skin surface generally covers an area of from a few square millimeters to a few square centimeters, and it may be curved rather than planar to accommodate concave or convex skin surfaces.

The surface of contact plate 44 that contacts a skin surface preferably is sufficiently smooth to permit the device to move over a skin surface without abrading it, even when the device is applied to the skin with pressure. The contact plate may further comprise handles (not shown) to be grasped by an operator while applying pressure when moving the device across the skin, or an attachment (not shown) for directly connecting the plate 44 to a laser apparatus.

In another embodiment shown in FIG. 25B, the covering is a coating 42 of a transparent index-matched liquid having sufficient viscosity that, when applied to the skin surface 12, will present a smooth surface to incident light beam C. When light is incident upon a smooth liquid coating applied over the surface of the skin, reflection losses are minimized. More light reaches the hair follicles beneath the coating than in the absence of the coating because the light is directed to the follicles in the path of the laser without redirection at the skin boundary. If light is directed perpendicularly to the smooth surface of the liquid covering, the light beam will pass directly into the skin without being redirected by refraction or scattering at the boundary of the skin as shown in FIG. 25B. However, scattering will occur once the light enters the skin.

Selection of the index of refraction of the liquid controls the transmission of light to the skin under laser treatment. For example, the liquid can be a transparent oil, such as mineral oil, which has an index of refraction of about 1.47 as compared with 1.37 for skin. The hydrating effect of the oil on the skin surface also improves the smoothness of the skin itself. In the case where the index of refraction of the oil is matched as closely as possible to that of skin, the liquid coating will form a smooth optical boundary between the incident light

and the skin to be illuminated. Alternatively, if the index is between that of air and of skin, the liquid will act as an antireflective coating to minimize reflection of incident light. The coating of a transparent liquid may need to be reapplied during the illumination phase if surface heating occurs.

5 In certain prior art hair removal procedures, the skin is pretreated with particles of an exogenous chromophore forced into hair ducts to provide a heat absorbing medium around the hair follicles. When the index-matched liquid covering is used in conjunction with this method of hair removal, once the chromophore particles are worked into the hair ducts, the carbon particles should be cleaned off the surface of the skin, *e.g.*, with a surfactant. A
10 surfactant helps to work the carbon into the hair follicles. Once cleaned, the area can be covered with a clear index matching coating of liquid and treated with the laser light. Optionally, the skin surface can be coated with the liquid covering of the invention and then the contact plate can be applied atop the smooth liquid coating, as shown in FIG. 25C. By this method, loss of light energy is minimized during transfer all the way through to the skin.
15 This sequence of steps will aid in concentrating the effects of the laser light on the hair follicle, thereby enhancing the treatment process.

 In yet another embodiment, the contact plate is incorporated within a domed reflector 48 as shown in FIGS. 26 and 27. In this embodiment, transparent contact plate 44 is a flat plate with smooth parallel sides, a light receiving side 52 and a skin-contacting side 54. The
20 skin-contacting side is smooth enough to move freely over a skin surface without abrading it.

 The domed reflector further comprises a thin transparent dome 56 joined to the transparent contact plate along the periphery of its light receiving side 52. The dome is a shell, and when attached to the contact plate, encloses or partially encloses, an interior void space. Preferably the contact plate is circular and the dome is hemispherical. A handpiece 58
25 can be attached to the dome to facilitate handling as shown in FIG. 27.

 The rounded interior surface 60 of the dome (*e.g.*, hemisphere) is covered with a coating 72 highly reflective to light at the wavelength of the laser. An opening is provided in the reflective coating at the apex 62 of the dome 56 through which incident light can pass. Alternatively, the dome has an aperture 64 located at its apex through which incident light
30 passes, and the interior surface of the dome is coated with the reflective coating. If the

contact plate is circular and the dome is hemispherical, the aperture is generally circular as well. The reflective coating can be made of any reflective substance, such as silver, depending on the laser to be used.

In use, as shown in FIGS. 26 and 27, the domed reflector 48 is placed atop a skin surface 12 to be irradiated, and light is directed to the skin through the domed reflector. The light enters the opening in the reflective coating of the dome, or through the aperture 64 at the apex of the dome, passes through the interior void space within the dome, and passes through the transparent, index-matched contact plate 44 to the skin surface 12. Any of the incident light photons 66 reflected or refracted away from a skin surface contacted by the skin-contacting side of the contact plate will be returned to the skin by the reflective coating on the interior surface of the dome. If the dome is hemispherically shaped, light reflected from the interior reflective surface of the dome will be reflected back to the skin near its point of origination. Thus the amount of light lost is decreased, and the efficiency of any laser skin treatment is increased.

The contact plate protects the reflective interior surface of the dome from contamination by particles of skin, *etc.*, that would be created by action of the laser upon an uncovered skin surface. In addition, the contact plate incorporated within the domed reflector will prevent laser action from exploding a chromophore off the skin surface during lasing. Further, the contact plate assists in forcing the chromophore particles into hair ducts or other skin structures during lasing.

In another embodiment, the scatter-reducing liquid coating is applied to the skin surface and the domed reflector is placed atop the liquid to direct any reflected light back to the skin (FIG.28). As in other embodiments of this invention, the liquid coating is index-matched to the skin so as to make a smooth optical boundary between the skin and the skin-contacting surface of the domed reflector. Alternatively, the skin surface is covered by an index-matched liquid and a contact plate with an antireflective coating on its smooth light receiving side is placed over the liquid on the skin surface for lasing (FIG. 25C).

The methods and devices of this invention provide the advantage of reducing loss of incident light at a skin surface, such as during the period of laser illumination for skin resurfacing, hair removal, or inhibition of hair growth. Use of a solid covering, *i.e.*, a contact

plate or a domed reflector, during such procedures offers further advantages. For example, pressure applied to the covering (*i.e.*, in a direction parallel to the direction of the laser beam path) and transferred to the underlying skin has a number of beneficial effects which aid in hair removal. The pressure compresses skin in contact with the covering device, thereby
5 effectively shortening the hair duct and/or the distance from the skin surface to the bottom of the hair follicle because the solid covering compresses the upper layers of the skin. Furthermore, shortening the distance the light must travel to reach the bottom of the hair duct decreases the attenuation of light traveling to the target cells. As a result, milder lasing conditions are required than when the covering is not used. A third effect of using the
10 covering devices during hair removal is that blood flow into the section of skin being illuminated can be restricted by compression of the capillary bed if pressure applied by the overlying device is greater than the patient's blood pressure. The restricted blood flow results in more effective delivery of laser light to the follicle and surrounding cellular targets, since blood can absorb a small fraction of the laser light. In addition, compression of the skin
15 surface by the device reduces scattering of light within the skin. All of these factors aid in accomplishing the goal of inhibition of hair growth while minimizing damage to the skin surface.

20 **No. 18: HAIR REGROWTH METHOD USING GRAFTING OF PAPILLA AND BULGE AREA STEM CELLS**

It is known that papilla and mid-derm bulge area stem cells play an important role in the hair growth cycle. Several groups of researchers have reported on the key role in regulation of hair growth found in bulge area stem cells. In electrolysis, for example,
25 particular attention is directed to destruction of hair stem cells. New ways of exploiting the key role of bulge area stem cells in stimulating hair growth are needed to combat alopecia, particularly male pattern baldness.

The present invention provides a method for utilizing an individual's undifferentiated papilla and/or bulge area stem cells to stimulate hair growth. The inventors have discovered
30 that bulge area stem cells can be harvested, isolated, cloned, and successfully transplanted

into an area of the donor's skin where increased growth of hair is desired to increase hair growth therein.

In the first step of the method, a donor section of skin is identified having growth of the type of hair for which increased growth at the recipient site is sought. Since hair types differ according to their anatomical site, it is generally desirable to match the hair produced by the donor stem cells to the type of hair that is desired at the recipient site. For example, in treatment of male pattern baldness, tissue samples are harvested from an area of the scalp that still exhibits vigorous growth. Once the donor site is identified, it is anesthetized locally using any convenient means and a plurality of tissue samples are obtained from the donor site. The tissue samples must contain hair follicles with intact undifferentiated papilla and/or dermal stem cells, as well as immediately surrounding tissues. Any method of tissue sampling can be employed, for example, punch biopsy, so long as viable stem cells can be obtained.

Undifferentiated stem cells are separated out from the mid derm bulge area of hair papilla in the tissue samples. For example, the tissue samples can be microsurgically dissected to locate and separate out the stem cells. The separated stem cells are then cloned by culturing them in an appropriate growth medium, such as Dulbecco's modified Eagle's medium (DMEM) with fetal calf serum, for a sufficient time to allow proliferation and differentiation of the cells.

Generally, the cells are cloned to a cell density of about 40 cells per cubic centimeter. A single growth cycle will require approximately 21 to 28 days. During culture, the medium is kept at about body temperature, or 37° C. One skilled in the art will understand that any one of a number of alternative growth media can be used to foster proliferation and differentiation of the stem cells. Once the desired cell density is achieved, for instance after about 2 to 3 passages, the cloned cells can be examined microscopically to detect the vital cells. Healthy differentiated stem cells are generally identified by applying a vital dye, such as Hoechst 33258 or Hoechst 33342 fluorescent dyes, incubating the cells for about 30 minutes, and then determining which of the cells fluoresce.

A sterile suspension of the cells in a biologically acceptable carrier medium, such as normal saline, is then prepared for inoculation or transplant into one or more recipient sites of

the same individual from which the stem cells were harvested. Suitable carrier media include aqueous or non-aqueous solutions, suspensions, and emulsions. Examples of non-aqueous solutions are propylene glycol, polyethylene glycol, and injectable organic esters, such as ethyl oleate. Aqueous carriers include water, alcoholic-aqueous solutions, and suspensions, including saline and buffered media. For interdermal grafting, the suspension of differentiated stem cells should be at a density of about 3 to about 10 percent by volume.

For grafting of the differentiated stem cells, the recipient site is prepared by scraping the skin surface and making superficial incisions of about 200 microns in depth. The solution of stem cells is delivered to the recipient site, generally by pipette, and the site is covered with a sterile bandage, such as Tegaderm™.

In an alternative embodiment, the solution delivered to the recipient site additionally contains polypeptides that trigger initiation of angiogenesis and neurogenesis, which are expressed into the media by the stem cells during the cell culture mitotic process.

If desired, a portion of the cloned stem cells can be frozen and reserved for future inoculation into the individual undergoing hair growth treatment. If frozen to a temperature of about -70° C, a bank of auto stem cells can be kept for several months, allowing for fast expansion in culture when required.

The method of the invention is illustrated in the following example:

1. Stem cells were collected by punch biopsy from 102 healthy hair root canal bulge areas of an individual to be treated, and the samples were micro-surgically dissected to separate out and collect the undifferentiated stem cells from the mid-derm bulge area of hair papilla.
2. The collected stem cells were placed for cloning into Dulbecco's modified Eagle's medium (DMEM) with fetal calf serum as a culture medium.
3. When cells had proliferated and differentiated (approximately 21-28 days per one cycle) to about 40 cells per 1 cm³, the healthiest were selected and separated into three groups.
4. One group was frozen to -70° C to create a bank of auto stem cells for fast reproduction when required. The second group was cloned in order for the

secondary population to reach the cumulative population doublings (CDP) required, usually 2 to 10 times.

5. The third group was used for the preparation of a sterile suspension of stem cells in a carrier medium. The suspension was inoculated interdermally by pipette into recipient sites prepared on the scalp of the donor individual. Alternatively, the suspension was applied topically to the area being treated for hair regrowth, along with polypeptides expressed into the media by the stem cells during the cell culture mitotic process.

6. The areas inoculated with hair stem cells experienced increased hair growth and hair regrowth after about 21 to 28 days.

The method of hair growth via cell transplant of this invention provides the advantage that cloned stem cells can be expanded in culture so that the amount of donor material to be transplanted is not limited by the number of cells that can be harvested. Thus an individual with relatively few donor sites can provide enough stem cells to stimulate hair growth in a large area of skin, if so desired. In addition, the cloned cells can be implanted into the recipient sites without making more than superficial surgical incisions in the recipient sites. In contrast, many prior art hair grafting procedures require use of more extensive surgical techniques to implant the donor tissue.

No. 19: METHOD FOR LASER REMOVAL OF HYPERTROPHIC AND KELOID SCARS

The majority of scars heal normally over time, presenting no additional difficulties. However, in certain instances healing proceeds abnormally, generating excessive or hypertrophic scar formation. Hypertrophic scars remain as raised, red, "angry-looking" tissue that does not fade over time. Keloids are scars that continue to enlarge, forming smooth, hard growths, often presenting a bulging, tumorous appearance. Keloids may develop on any part of the body, although the upper chest and back are especially prone to keloid formation. Keloids occur more frequently in heavily pigmented individuals.

Recently, it has been reported that postoperative low megavolt electron beam irradiation is effective in the prevention or recurrence of hypertrophic scars and keloids

(*Radiotherapy and Oncology*, 19 (1990) 267-272). Keloid and hypertrophic scar treatment using a carbon dioxide laser has also recently been described (Stern and Lucente, *Arch Otolaryngol Head Neck Surg* Sep 11, 5:9:1107-11, 1989); however, a recurrence rate of approximately 70% following CO₂ laser therapy was reported. Accordingly, it would be
5 advantageous to have new and better methods of laser treatment for the removal of keloids or hypertrophic scars.

The present invention provides a method for removing keloid and hypertrophic scars by applying a light-absorbing contaminant to scar tissue to be removed so as to cause the contaminant to infiltrate the surface layers of the scar, and then illuminating the contaminated
10 scar tissue with short pulses of light well absorbed by the contaminant, but which pass through normal skin tissue with minimal absorption. The inventors herein have discovered that repeated treatment of a scar with laser light will cause growth of normal epithelial cells in the area where the scar appeared. The method used is as follows: a contaminant is applied to keloid or hypertrophic scar tissue, and the area is irradiated by laser energy for about 5 or 6
15 passes, or until erythema or minor inflammation is detected in the scarred area. Then a period of about 4 to about 6 weeks is allowed to pass before the treatment is repeated. A total of from about 2 to about 8 treatments, for example about 4 to about 6 treatments, is generally sufficient to cause reorganization of the epithelial layer and removal of the scar. A new layer of skin with the appearance and elasticity of normal skin will form. By a mechanism yet
20 unknown, the combination of the photochemical and photothermal effects caused by absorption of laser energy in the contaminant and/or the scar tissue and underlying tissue results in (1) disappearance of the scar and (2) formation of new spindle-type collagen fibers in the underlying dermis at the place where the scar had been.

The contaminant preferably comprises a light-absorbing chromophore of the type
25 known to be useful in laser hair removal procedures, such as a suspension of carbon particles in an oil- or water-based medium. The short pulses of light are provided by a light beam with a wavelength that is well absorbed by the contaminant, but which has minimal absorbence in skin. For example, a Nd:YAG laser with a wavelength of 1064 nm can be used in the practice of this invention. The contaminant is applied to the scar tissue so as to cause penetration of
30 the contaminant around and between the cells in the upper layer of the scar tissue. Brisk

massage or ultrasound can be used to force the contaminant under and between cells on the surface of the scar tissue.

The laser parameters and size of the particles in the contaminant should be selected so as to assure that the particles in the contaminant will explode upon illumination with short pulses of light. Some of the particles on the surface of the skin will be forced into the skin as a result of the shockwaves resulting from the explosion of other particles. In addition, the pulses of light interact with the skin and the particles below the skin. The particles below the skin surface that explode or vaporize upon illumination will rip off the layers of the hypertrophic scar or keloid which lay above the exploding particles. The pulses are continued until essentially all of the chromophore particles are exploded. This procedure should be repeated until sufficient layers of hypertrophic scar or keloid have been removed to remove the appearance of the scar.

Laser energy not absorbed in the contaminant is harmlessly dissipated in the skin and surrounding tissue. There is generally minimal pain or feeling of heat, and no significant injury to the skin tissue. It is preferable to provide a slight diverging beam to assure that the beam spreads before it hits the skin. For example, in one embodiment, the spot size of the light beam at the skin surface is about 0.5 cm in diameter and, before interacting with the skin, the beam spreads at an angle from the vertical of about 10 degrees. Post-operative treatment of the targeted area includes any commonly accepted methods known to those in the medical arts.

While the invention is illustrated with reference to the combination of a Nd:YAG laser and a contaminant containing carbon or graphite particles, persons skilled in the laser-medical arts will recognize that many other laser-contaminant combinations can be used to practice this invention. The important attributes of the combinations are:

- The contaminant must absorb light energy well at the wavelength of the laser beam.
- The laser beam must be a pulsed beam with very short pulses (pulse durations of less than 1 microsecond.
- The contaminant must be capable of being infiltrated into the upper layers of the scar tissue.

- The contaminant must explode with sufficient energy to tear off cells of the scar tissue upon absorption of the laser energy.
- The treated area must have about 2 to 8 treatments spaced at intervals of about 4 to 6 weeks wherein during each treatment the area is irradiated by laser energy for about 5 or 6 passes, or until erythema or minor inflammation is detected in the scarred area

Upon laser treatment as described herein, treated scars are substantially removed, and new spindle-type collagen fibers are formed in the underlying dermis of the targeted area. It is also notable that turgor of the skin is restored at the location where the scar had been prior to the laser treatment. Such results suggest that laser treatment of the afflicted area stimulates reorganization of tissue. According to Goslen (*Physiology of wound healing and scar formation*. In: Thomas, J.R. et al., eds. *Facial Scars - Incision, Revision, and Camouflage*. St. Louis: CV Mosby, 1989), wound repair progresses normally through the following five stages: a vascular phase, an inflammatory phase, a re-epithelialization, formulation of granulation tissue, and remodeling of matrix and collagen. The final phase of wound healing, matrix and collagen remodeling, begins as water is resorbed from the scar due to the replacement of hyaluronic acid by proteoglycans. Cross-linking of collagen fibers proceeds by lysyl oxidase. Type III collagen is catabolized and replaced by type I, and the collagen bundles are reoriented to lie parallel to the skin surface. The metabolic aberration which leads to keloid formation is believed to occur in this late phase of scarring when keloids fail to mature and become compacted. Apparently, by some presently unknown mechanism, the present method of laser treatment returns the afflicted area to a state of wound healing such that in the final phase of wound repair appropriate collagen formation occurs, substantially avoiding formation of subsequent scars.

This invention provides a method of laser-assisted scar removal without surgery. Because the treatment stimulates reorganization of tissue to promote proper healing, the likelihood that hypertrophic or keloid scars will reform is substantially reduced over the prior art methods of removing scar tissue. Since the majority of the laser energy is absorbed by the contaminant, rather than skin tissue, the risk of damaging healthy tissue is reduced over methods which use a laser beam that is well absorbed in tissue.

**No. 21: HAIR REMOVAL USING HAIR BLOOD SUPPLY COAGULATED
BY PHOTONS GUIDED BY A LIGHT-GUIDING FLUID IN HAIR
DUCTS**

Hemoglobin in blood is a naturally occurring chromophore useful in hair removal techniques. Hair follicles are fed by a network of fine capillaries and blood vessels concentrated at the base of the follicles. U.S. Patent Number 4,388,924 issued June 21, 1983 to Weissman *et al.* discloses a method of depilation comprising directing laser energy with a wavelength of approximately 4800 to 5200 angstroms via a laser transmitting probe through the skin to terminate at the base of a hair follicle so as to devitalize the hair by coagulating the blood vessels at the hair root. However, in the Weissman method the depilation is performed one hair follicle at a time, rather than by applying the laser to a skin section containing a multiplicity of hairs for simultaneous treatment. More efficient ways of utilizing the natural chromophore in blood for inhibiting hair growth are needed.

In this invention the combination of absorption coefficient and photon wavelength used for laser hair removal is selected so as to accomplish selective photocoagulation of the blood vessels at the end of hair follicles that have been filled with a light guiding medium, such as mineral oil, to guide photons to the hair roots. In this embodiment of the invention, an external chromophore is not infiltrated into hair ducts to absorb the energy of the laser light. Instead, the naturally occurring chromophores in blood are the target to which a laser is tuned. A combination of absorption coefficient and photon wavelength is selected to assure absorption of sufficient energy by blood chromophores in capillaries at the bottom of the hair follicle to heat the blood in the capillaries and surrounding epithelial tissue to a temperature of about 70° C to about 80° C for 0.1 to 1.0 second, with the shorter time corresponding to the higher temperature.

The wavelength of the laser is selected to be well absorbed in blood chromophores, but with a minimum of absorption in skin tissues. Blood absorbs photons strongly at about 400 nm with an absorption coefficient of about 2000 cm⁻¹, and blood vessels can be easily coagulated by photons having a wavelength of about 400nm to about 1300 nm, for example 400nm to about 650nm. Moreover, photons within this wavelength range cannot penetrate

deep into the dermis. Therefore, use of laser light within this range of wavelengths will coagulate the blood vessels at the base of the hair root, but will not destroy blood vessels below the epidermal layer of the skin.

However, a large proportion of light at the above wavelengths will not penetrate directly through skin to the capillaries at the base of hair roots. To overcome this problem, a portion of the light incident on the skin surface is delivered to hair roots via hair ducts filled with a light-guiding liquid. Preferably hairs are removed from hair ducts in the skin section to be treated before the hair ducts are filled with a light guiding liquid.

The preferred light guiding liquid is relatively transparent to light and has an index of refraction greater than that of skin so that a photon entering the light guiding liquid in the hair duct is transmitted there through by continuous internal reflection. For example, experiments have been conducted using mineral oil (index of refraction of about 1.47) as a light guiding liquid. These studies indicate that mineral oil is relatively transparent to light having a wavelength in the range from about 400nm to about 650 nm. In addition, because the index of refraction of mineral oil is substantially greater than that for skin (index of refraction of about 1.37), an oil-filled hair duct will conduct light beams down the hair duct to the papilla area by continuous internal reflection, operating much the same as a fiber optic. This effect is illustrated in FIG. 29, which shows the path of a typical photon 1 traveling down the hair duct 31 through the light guiding fluid 68, similar to photons in an optical fiber, and being absorbed in blood vessels 70 at the bottom of the hair duct. Other photons that do not strike the light guiding fluid will be absorbed (photon 1) or scattered by epidermis 12.

The chromophores in the blood vessels that feed hair follicles thus receive illumination both from photons that penetrate and are scattered by the dermis, and from photons traveling down through the light guiding liquid in the hair duct. The laser is preferably operated in the continuous wave (CW) mode, and the power is set such that the temperature rise of blood at the hair root is high enough to denature the capillaries, but below the threshold for vaporization of the tissue, so that the light guiding liquid will not be boiled or blown out of the follicles.

The preferred steps to be followed in practicing this invention generally comprise the following:

1. Hairs are optionally extracted from the follicles to be treated using any known method, such as tweezing, waxing, *etc.*
2. A light-guiding liquid having an index of refraction higher than that of skin, such as mineral oil, is applied to the skin surface and worked into hair ducts in the region to be treated for inhibition of hair growth. If possible, the hair follicles should be filled throughout with the light guiding liquid. However, partially oil-filled follicles are also effective to deliver the light into hair ducts.
3. The surface of the skin is optionally precooled prior to application of the laser using any of the methods disclosed herein or known in the art.
4. A skin section containing a multiplicity of oil-filled hair ducts is illuminated with short pulses of laser light that is well absorbed by naturally occurring chromophores in blood.

It has also been discovered that inhibition of hair growth can be performed without aid from an exogenous chromophore by illuminating a section of skin containing hair ducts with short pulses of light at low fluence having a wavelength of about 1064 nm, such as is provided by a Nd:YAG laser. Using a light-guiding liquid in the hair duct is optional in this embodiment of the invention. It has been discovered that the skin contains naturally occurring chromophores and/or skin structures other than melanin that absorb light from a Nd:YAG laser at a wavelength of about 1064 nm.

A skin section containing hair ducts is illuminated with short pulses of low fluence light in a beam spot size of from about 7 to 10mm in cross-sectional dimension from a Nd:YAG laser at about 1064 nm wavelength. The fluence of the light is in the range from 0.1 to about 10J/cm² and pulse duration is about 900 μ s to about 8ns, for example, less than 1 μ s. Tissue associated with hair growth cells is affected (*e.g.*, ablated) such that hair growth is inhibited without unwanted damage to skin tissue. The preferred fluence range is less than about 7 J/cm², for example about 1 to about 3J/cm². When parameters in these ranges are used to illuminate the surface of a section of skin containing hair ducts, naturally occurring chromophores in proximity to hair growth cells in hair ducts absorb the short pulses of light and transfer energy to the hair growth cells so as to inhibit hair growth. Regrowth of hairs

from skin sections treated according to this embodiment of the invention is substantially impaired.

Low fluence Nd:YAG illumination can also be used to perform laser-assisted skin rejuvenation without use of an exogenous chromophore. The laser parameters are the same as for hair removal except that the beam spot size is smaller to target the beam more shallowly, for example to a depth of about 100 to 200 microns.

The following examples illustrate the manner in which the invention can be practiced. It is understood, however, that the examples are for the purpose of illustration, and the invention is not to be regarded as limited to any of the specific materials or conditions therein.

Example 6

Blood coagulation is accomplished using a laser with a wavelength of 415nm, a pulse duration of about 1 ms, and energy density of about 0.6 J/cm². This laser can be a dye laser.

Example 7

Blood coagulation is accomplished using a laser at about 532 nm with a pulse duration of about 100 μ s, and energy density of about 5 J/cm². This laser can be a KTP solid state laser with a wavelength of 532 nm

The calculated increase in temperature in blood in a 5 μ m blood vessel and surrounding tissue one blood vessel radius away from the wall corresponding to irradiation of a skin surface with a short pulse laser is shown in FIGS. 30A and 30B. FIG. 30A shows the calculated temperature rise at the center and wall of a blood vessel as well as in the surrounding tissue when illuminated by photons at 415 nm wavelength with 0.2 J/cm² fluence and pulse duration of 100 μ s. FIG. 30B shows the similar values for 0.6 J/cm² fluence and a pulse duration of 1ms. This calculated data shows the instantaneous temperature rise in blood. At both fluences, the increase in temperature over normal body temperature is of sufficient duration to cause permanent damage to epithelial cells. FIG. 31 shows the corresponding increase in skin temperature beneath the skin surface when the skin surface is maintained at 0 °C by cooling. With pulse durations longer than 100 μ s, the temperature rise at the interface of

the epidermis and dermis, where skin melanosomes are located, is very small so there is little risk of their destruction.

The present invention affords several advantages over prior art methods of laser assisted inhibition of hair growth. First, a naturally occurring chromophore is irradiated by the laser and used to selectively denature the blood vessels that feed hair follicles. In the method of this invention, the laser fluence needed to coagulate the blood vessels that feed hair ducts is very low. In addition, since blood absorbs light waves at a frequency that is poorly absorbed in skin, there is reduced risk of unwanted damage to skin tissue or pigmentation.

No. 22: HAIR REMOVAL BY COMBINATION OF LONG PULSE LASER WITH SKIN COOLING

There can be some disadvantages of using short pulse lasers for hair removal. Because the energy is transmitted so quickly into light absorbers, the light absorbing medium can be vaporized. The heat of vaporization consumes a large portion of the energy, with little energy remaining for transfer by thermal conduction to the target tissue. Even if the surface of the skin is precooled, short pulse lasers can burn the skin. In addition, short pulses of laser light may cause pinpoint bleeding from the blood vessels in the upper dermis, or these blood vessels may be coagulated. Another danger is that short pulse lasers can vaporize the melanosomes at the interface of the epidermis and dermis, resulting in unsightly destruction of normal pigmentation of the skin. These problems are overcome in the present invention by using long pulse lasers in combination with dynamic cooling of skin.

Selection of pulse duration for laser skin treatment is important for controlling the amount of unwanted damage that is suffered in order to attain a desired goal. Laser hair removal techniques in which an exogenous chromophore is infiltrated into hair follicles present unique problems in the selection of pulse duration because of the difficulty of driving exogenous chromophore particles throughout hair ducts.

The present invention provides an improved method for inhibiting the growth of unwanted hair using an exogenous chromophore, such as carbon particles, infiltrated into hair ducts. The method combines the use of a long laser pulse with dynamic cooling of the skin

surface. The pulse of light used to heat the contaminant is long enough to avoid exploding and/or vaporizing the particles. The laser parameters are selected to provide a long pulse of light at sufficient power to heat the tissue surrounding the base of the hair follicle so as to cause tissue damage. To avoid concurrent damage to other skin tissue, the surface of the skin, which is at or near body temperature at the beginning of the process, is precooled. Cooling is continued throughout the illumination of the skin with a single long pulse of laser light. Then the skin surface is allowed to return to normal temperature before the three step process of precooling, heating while cooling, and return to starting temperature is repeated.

Precooling of the skin surface establishes a steep temperature gradient within the skin, with temperature increasing at increasing skin depth. Preferably the precooling flux is sufficient to equilibrate the temperature of the skin surface to that of the cooling flux while allowing the temperature at the depth of the hair root to remain at body temperature. For example, a 1 second exposure of the skin surface using a coolant at 0° C should have sufficient flux to drop the surface temperature to about 0° C. If the same cooling flux is continued during the long laser pulse, the surface of the skin will remain at about 0° C, but the skin temperature with depth will increase over that established during the precooling step. At the depth of the hair roots, the temperature should increase to about 70° C to 80° C for about 0.1 second. At about 50 to 100 microns depth, the level at which the melanosomes are found, the temperature should not rise to more than about 50° C to avoid damage to skin pigmentation.

A "long" laser pulse, as used herein, is defined with reference to the type and size of the chromophore particles illuminated and the wavelength of light used. Functionally, a long pulse is a pulse long enough to substantially avoid exploding or vaporizing chromophore particles infiltrated into hair ducts. The invention is illustrated with reference to light at a wavelength in the range of from about 600 nm to about 1100 nm and carbon or graphite particles in the size range of about 10nm to about 1 μ m. At this wavelength and particle size, a long pulse has a duration of from about 100 μ s to about 100 ms. Alternatively, as used herein a long laser pulse can be a train of shorter pulses in such rapid succession that the interval between the end of one pulse and the beginning of the next pulse is less than the average thermal relaxation time of the chromophore particles. Such a train of short rapid

pulses approximates the characteristics of a single long pulse. For example, at the above wavelength and carbon particle size, a train of shorter pulses having a pulse duration of about 1 ms to about 10 ms separated by about 1 ms can be substituted for a single pulse having a duration longer than the pulse width of a single pulse in the pulse train. A chopped CW laser is also considered a "long" pulse laser as the term is used herein.

A "long" pulse laser is one which releases its energy over a sufficient period of time that a light-absorbing chromophore surrounded by skin tissue, for example in a hair duct, has time to transfer energy from the chromophore to the surrounding tissue during the pulse. Because heat flows out of the chromophore into surrounding tissue, explosion of the chromophore particle is avoided. Generally, to denature the immediately surrounding tissue, the transfer of heat should be sufficient to raise the temperature of tissue immediately surrounding the base of the hair duct to about 70° C to about 80° C for a period of from 0.1 to 1 second for a radial distance of no more than about 60 microns from the wall of the hair duct. It should be particularly noted that as the pulse duration increases, the laser energy required to accomplish the requisite heating and the distance to which the target temperature extends is increased. Therefore, for carbon particles having an average diameter from about 10 nm to about 1 μ m, a fluence of about 15 J/cm² is used with a pulse duration of about 100 μ s, while a fluence of about 30 J/cm² is used with a pulse duration of about 100 ms. At a fluence of about 30 J/cm² and pulse duration of about 100 ms, tissue will be denatured for a radial distance of about 60 microns from the wall of the hair duct. Further increase in the distance to which tissue is denatured is generally not necessary or desirable for the purposes of inhibiting hair growth.

Due to the steep temperature gradient established by precooling the skin surface and the continued application of the cooling flux during a long pulse illumination, the temperature of the epidermis and upper dermis is kept cool enough during the laser pulse to avoid damage, while the temperature of the tissue surrounding a hair duct at the depth of the hair root increases sufficiently to inhibit future hair growth. Thus, selective damage of hair follicles can be achieved during laser hair removal without undesirable damage to other skin structures.

FIG. 32 shows the calculated temperature rise in tissue surrounding a hair follicle that is filled with carbon/oil lotion and illuminated with a 60 W/cm^2 Nd:YAG laser (1064 nm) for 0.1 second. The hair follicle is considered as an infinitely long cylinder with a radius of $a = 25 \mu\text{m}$. It is assumed in the calculation that the follicle is filled with enough carbon particles so that essentially all photons striking the follicle are absorbed. As seen from FIG 32, the temperature of the tissue between the wall of the follicle and one radius away from the wall is over 70°C for a period of about 0.1 second, which is enough to thermally kill the cells in the tissue. The goal of long term inhibition of hair growth is achieved when tissue up to one radius length away from the wall of the hair duct is thermally damaged.

Because of absorption and scattering of photons by tissue, the photon flux distribution in skin decays approximately exponentially with depth. The light intensity at 3 mm depth may be only 25% of the incident flux. It has been discovered that the power density of incident light should be 240 W/cm^2 in order to have 60 W/cm^2 at 3 mm depth, the average depth of hair follicles in an average section skin. However, a skin surface illuminated with 240 W/cm^2 fluence of 1064 nm wavelength laser for 0.1 second will be burned unless cooled. To succeed in providing sufficient power to the chromophores at the base of the hair follicle without burning skin tissue, other than that immediately surrounding a hair duct, dynamic cooling is applied to the surface of the skin section that is being illuminated. For example, in one embodiment the contaminant contains carbon particles in a size range from about 10nm to about $1 \mu\text{m}$, the laser wavelength is in the range of 600 nm - 1100 nm, the pulse duration varies from $100 \mu\text{s}$ to 100 ms, and the laser energy range is from 3 J/cm^2 to 30 J/cm^2 depending on the pulse duration. The longer the pulse duration, the higher the laser energy required. A pulse duration of about 100 ms is preferred.

The area of skin surface that needs to be cooled is the area that is being illuminated. Therefore, the cooling medium can be applied directly onto the skin surface where the treatment for hair removal is sought. For example, the cooling effect can be accomplished by applying to the skin surface a continuous spray of ice water or other coolant that will be capable of bringing the surface of the skin to a temperature in the range from about 0°C to about 10°C when the cooling medium is applied for from about 1 to about 5 seconds. FIG. 33 above shows skin temperature at three different depths from the surface when the skin

surface is cooled to 0° C for 2 seconds. After exposure of the skin surface to 0° C for 2 seconds, temperature in the epidermis and upper dermis is lowered significantly from body temperature, but the lower dermis remains at a temperature almost equivalent to body temperature, as shown in FIG. 34.

An environmentally compatible Freon™ substitute, such as tetrafluoroethene, is also suitable for this purpose. Alternatively, a cooling device designed to cool the surface of the skin during lasing can be used to administer a comparable cooling flux to the section of skin during lasing. Such a device is disclosed in co-pending U.S. Application Serial No.

_____, filed on even date with this application, which is incorporated herein by reference in its entirety.

Further methods of skin cooling are disclosed in Section No. 2 above.

In summary, the method of the invention is a three step process as follows:

1. A cooling flux is applied to section of skin sufficient to precool its surface to about 10° C to -10°C prior to illumination. Generally, the precooling period is from 1 to 5 seconds, for example one second.
2. A cooling flux is maintained on the surface of the skin section throughout a single laser pulse. Generally the cooling flux used during the precooling step is continued during a single long pulse of the laser. The duration and energy of the long pulse is sufficient that energy absorbed by the contaminant and transferred to tissue immediately surrounding the base of a hair follicle in the section of skin destroys hair growth cells therein despite the temperature gradient in the skin established by the precooling and cooling maintained during the laser pulse. Generally, tissue within about 1 to 2 follicle widths from the wall of the hair duct (or about 30 to about 60 microns) is heated to a temperature from about 70° C to 80° C for a period of about 0.1 second by heat transferred from the contaminant during a single laser pulse, which is about 0.1 second in duration. The cooling flux on the skin surface is maintained throughout the laser pulse to protect tissue further than about 1 to 2 follicle radii from the wall of the hair follicle from damage.

3. At the conclusion of the pulse, the cooling flux is terminated and the surface of the section of skin is allowed a rest period to return to body temperature before the three-step process is repeated.

A total of 1 to 3 treatments is generally sufficient to cause long term inhibition of hair growth in a section of skin treated using the above method. Rather than ceasing the laser treatment during the rest period, it is generally convenient to use the three-step cycle in treatment of a different section of skin during the rest period, so long as the new section of skin is about body temperature at the start of the three-step process. If the circumference of the cooling zone is substantially the same size as the spot size of the laser beam, an adjacent skin section may be at body temperature within less than a second following the conclusion of the laser pulse. In any event, it may be convenient to program a laser to move automatically from skin section to skin section in a predetermined pattern so that an area of skin containing several skin sections (each one of which may be no larger in area than the beam spot size) is scanned in an orderly pattern, moving through the pattern from one to about three times as needed to accomplish the goal of inhibiting hair growth without undesirable damage to skin tissue.

The present invention advantageously avoids production of kinetic energy generated by exploding or volatilizing exogenous chromophore particles in a hair duct, which can damage the natural chromophores at the meeting point of the epidermal and dermal layers, thereby disrupting the pigmentation of the skin surface. In addition, pinpoint bleeding in the skin is avoided. The present invention provides the advantage that these risks are completely avoided by utilizing a long laser pulse in combination with dynamic skin cooling.

This aspect of the invention having been fully described, it is further illustrated by the examples below.

Example 8

Sample calculations were performed utilizing a precooling flux applied to the surface of the skin section sufficient to attain a temperature of about 20° C at a depth of about 500µm below the surface of the section of skin within two seconds. If this cooling flux was maintained during a long pulse of laser light (60 W/cm², Nd:YAG laser at wavelength of

1064 nm, pulse duration of 0.1 second), the temperature of the tissue surrounding the contaminant filled hair duct increased to a temperature of about 70° C to about 80° C for a period of about 0.1 second. This temperature increase is sufficient to destroy the cells, but higher fluence is need for damage to follicular tissue at a depth of 3 to 4 mm, as discussed above.

Example 9

For comparison, similar calculations were made using the same laser cooling regimen and parameters (60 W/cm², Nd:YAG laser at wavelength of 1064 nm, pulse duration of 0.1 second) to determine the temperature rise of blood vessels in the upper dermis and in melanosomes at the interface of the epidermis and dermis. These calculations showed that the temperature rise of blood vessels with a diameter smaller than 50 μ m is less than 20° C under the above laser conditions. Further calculations showed that under the same conditions the heat generated in an individual melanosome of 1 μ m diameter located at the interface of the dermis and epidermis by a laser pulse with a duration of 0.1 second is dissipated into the surrounding tissue without substantial increase of temperature over that of the surrounding skin tissue. Hence with continuous cooling of the skin surface during each laser pulse, as described above, the tissue in and surrounding a contaminant-filled hair duct can be selectively coagulated without unwanted burning of skin, or damage to blood vessels and skin pigmentation.

No. 21: USE OF RADIO WAVES TO CONTROL HAIR GROWTH

It is known to use various wavelengths of light in skin treatments and to cause inhibition of hair growth. Use of other types of electromagnetic radiation would enhance the choices, allowing the practitioner to select the type of radiation best suited to a particular task.

This aspect of the invention provides a system for encouraging or retarding hair growth. Referring now to FIG. 36, a section of skin 100 includes one or more hairs 102 growing from follicles 104 in hair ducts 106. Metallic particles 108, for example, nanophase

iron particles, are applied to the skin surface 110. Particles 108 may be applied as a powder, in a solution or in a lotion formulated for topical application.

Referring now to FIG. 37, particles 108 are urged to enter hair ducts 106 and move down to follicles 104. In the illustrated embodiment, particles 108 are iron particles, which are ferromagnetic. A magnet 112 is used to apply magnetic repulsion to encourage at least some of particles 108 to enter hair ducts 106 and move down towards follicles 104. Alternatively, skin section 100 can be gently massaged to encourage particles 108 to move toward follicles 104 at the bottoms of hair ducts 106. After particles 108 have been worked into hair ducts 106, skin section 100 can be wiped and gently washed clean to remove excess particles from surface 110.

Referring to FIG. 38, a system for heating particles 108 in ducts 106 includes a radio frequency (RF) antenna array 114, an associated power supply 116, and a scanning mechanism 118 for scanning RF emissions from antenna over skin section 100. Scanning mechanism 118 can be a mechanical system that moves antenna array 114, or an electronic system that oscillates power applied from supply 116 to antenna array 114.

The RF radiation from antenna array 114 is absorbed by particles 108, which heats them. Particles 108 conduct heat to surrounding tissue in follicle 104. The radiation can be tuned and scanned across skin section 100 in a manner that converges the radiation at a carefully selected depth in skin section 100, generally from 1 mm to about 4 mm below the surface of the skin. This enables the system to target damage to follicular cells in predetermined regions 120 of follicles 104. Depending on the phase of growth, thermal damage to follicle cells may activate or retard hair growth.

Any metallic material or organometallic compound that absorbs RF radiation can be used in practice of the invention, including those in solution or as a free compound. Although RF radiation is well suited for heating nanophase iron particles, other types of radiation, such as microwave, and other frequencies that are matched to a particular metallic material or organometallic compound may also be employed. Particle sizes are not restricted to nanometer sizes. Particle sizes can include all sizes that can infiltrate the follicle and that, when combined with a suitable electromagnetic radiation, can provide focused heat in hair follicles 104.

A number of embodiments of the present invention have been described. Nevertheless, it will be understood that various modifications may be made without departing from the spirit and scope of the invention. Accordingly, other embodiments are within the scope of the following claims.

WHAT IS CLAIMED IS:

- 1 1. A method for inducing hairs into synchronized hair growth in a region of skin prior to
2 hair removal including applying a shocking agent or action to the skin region to shift the
3 phase of hair into the anagen phase prior to hair removal.
- 1 2. A mask for use during an illumination step in a hair removal treatment including an
2 opaque body with a planar surface area and having light-transmissive apertures disposed
3 there through such that the body blocks substantially all light photons except those
4 traveling perpendicular to the planar area.
- 1 3. A method for controlling the proportion of mechanical to thermal damage administered to
2 skin tissue surrounding hair ducts during illumination of chromophore particles within
3 the hair ducts to effect long term prevention of growth of unwanted hair on a section of
4 skin, the method including the steps of:
 - 5 (a) infiltrating into hair ducts in a section of skin a first portion of particles of a chromo-
6 phore having a size selected to ensure explosion of said first portion of particles upon
7 irradiation by short pulses of light at a wavelength absorbed by the chromophore;
 - 8 (b) infiltrating into said hair ducts a second portion of particles of the chromophore
9 having a different size selected to ensure transfer of heat to skin tissue surrounding
10 said hair ducts without explosion of said second portion of particles when illumi-
11 nated by said short pulses of light; and
 - 12 (c) illuminating the skin section with said short pulses of light, whereby mechanical
13 damage is caused to skin tissue surrounding said hair ducts in proportion to the first
14 portion of the particles in said hair ducts, and thermal damage is caused to skin tissue
15 surrounding said hair ducts in proportion to the second portion of the particles in said
16 hair ducts.

- 1 4. A method for controlling the proportion of mechanical to thermal damage administered to
2 skin tissue surrounding hair ducts during illumination of a chromophore particle within
3 hair ducts therein to effect long term prevention of growth of unwanted hair on a section
4 of skin, the method including the steps of:
- 5 (a) infiltrating a contaminant including light absorbing chromophore particles into hair
6 ducts in a section of skin; and
- 7 (b) illuminating the skin section with a combination of long and short pulses of light at a
8 wavelength well absorbed by the particles, said short pulses of light having a pulse
9 duration selected to cause a first portion of the particles to explode, and said long
10 pulses of light having a pulse duration selected to avoid explosion of a portion of the
11 particles;
- 12 whereby mechanical damage is caused to skin tissue surrounding said hair ducts in
13 proportion to the number of the short pulses in the combination, and thermal damage is
14 caused thereto in proportion to the number of long pulses in the combination.
- 1 5. A method for inhibiting the growth of hairs in hair ducts in a section of skin including
2 applying a hair growth-inhibiting amount of an anti-proliferative agent to the section of
3 skin so as to cause entry of the agent into hair ducts located therein, whereby growth of
4 said hairs is inhibited.
- 1 6. A method for tailoring laser assisted hair removal to an individual including:
2 (a) determining the current phase of hair growth for a majority of hairs in a region of
3 skin to be treated;
- 4 (b) selecting a wavelength of light best absorbed by the individual's hair color;
- 5 (c) selecting a light energy level for illumination depending upon the average depth of
6 hair follicles in the region and the current phase determined in step (a); and
- 7 (d) illuminating the region with the above-selected wavelength and energy level so as to
8 inhibit hair growth therein.

- 1 7. In a laser-assisted hair removal method, wherein a region of skin having one or more
2 follicles is illuminated with pulses of light to cause thermal damage, an improvement
3 including applying an illumination beam with a square or circular shape, said beam being
4 no wider than 8.0 mm at its widest point.
- 1 8. A method for the removal of hypertrophic or keloid scars including:
2 (a) coating a hypertrophic or keloid scar with a light-absorbing contaminant;
3 (b) illuminating the contaminated scar with short pulses of light preferentially absorbed
4 by the contaminant so as to selectively remove the scar.
- 1 9. A method for inhibiting growth of hairs in a section of skin including:
2 (a) filling hair ducts in the section of skin with a light guiding fluid; and
3 (b) illuminating the section of skin with light preferentially absorbed by blood so that a
4 portion of the pulses of light are directed to blood vessels at the base of the hair ducts
5 by the light-guiding fluid in the hair ducts.
- 1 10. A method for inhibiting growth of hairs in hair ducts on a section of skin including:
2 (a) applying a light absorbing contaminant to the section of skin so as to fill spaces in
3 the hair ducts;
4 (b) precooling the surface of the section of skin to about 10° C to -10° C ;
5 (c) illuminating the precooled section of skin with a single long pulse of light preferen-
6 tially absorbed in the contaminant while maintaining the cooling flux to the skin
7 surface throughout the pulse such that tissue at a radial distance greater than about 1
8 to 2 hair follicle widths from the hair ducts rises to no more than about 10° C above
9 body temperature during the single long pulse; then
10 (d) allowing the surface of the section of skin to attain body temperature; and
11 (e) repeating steps (b) through (d) for a total of 1 to about 5 times;
12 whereby tissue surrounding the hair ducts in the section of skin is selectively damaged
13 without substantial permanent damage to the appearance of the skin surface.

- 1 11. A method of controlling hair growth in a skin section that includes hair growing from
2 follicles in hair ducts, including:
- 3 (a) applying a material to the skin section, the material including metallic particles that
4 are capable of entering hair ducts;
- 5 (b) urging at least some of the particles to enter the hair ducts and move to the follicles;
6 and
- 7 (c) applying to the skin section electromagnetic radiation having a frequency that is
8 absorbed by the metallic particles so as to heat the particles and cause damage to
tissue surrounding the hair ducts.

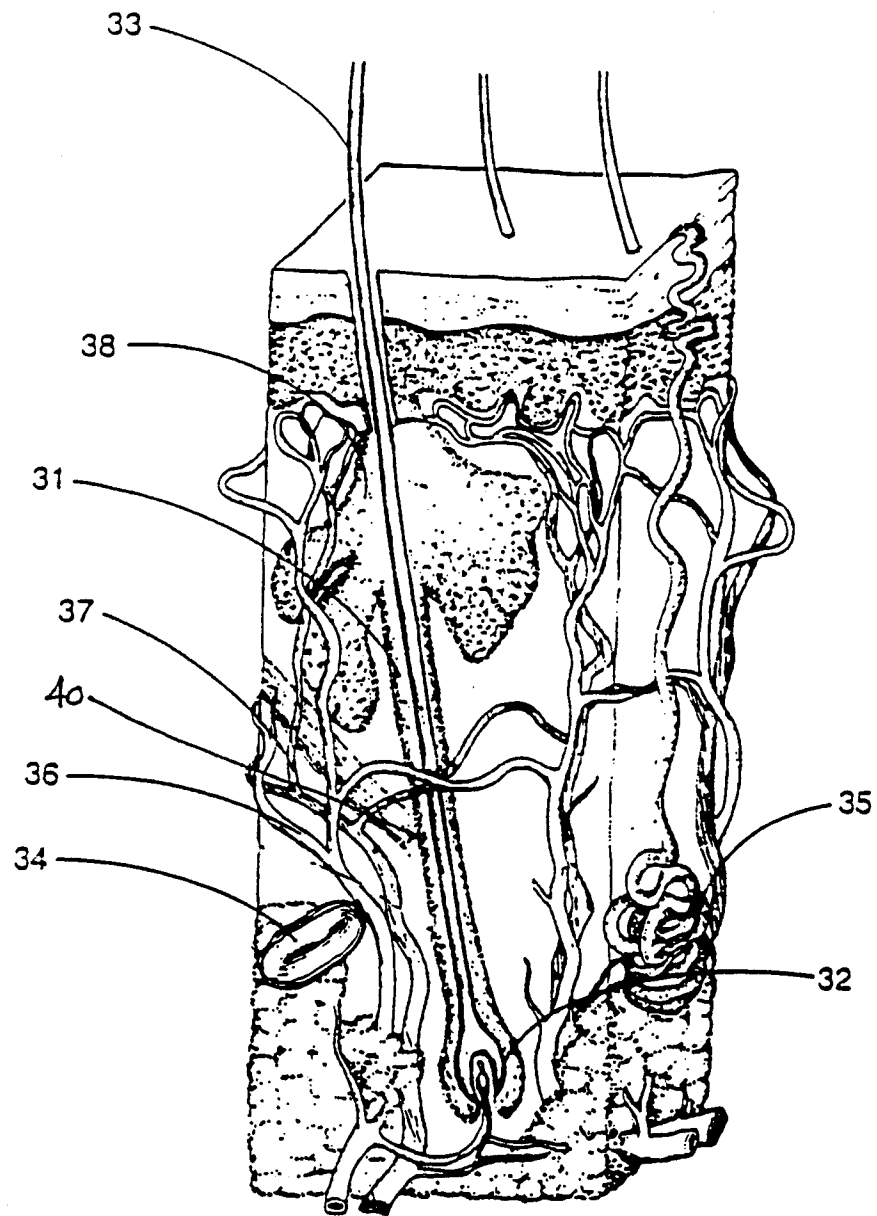


FIG. 1

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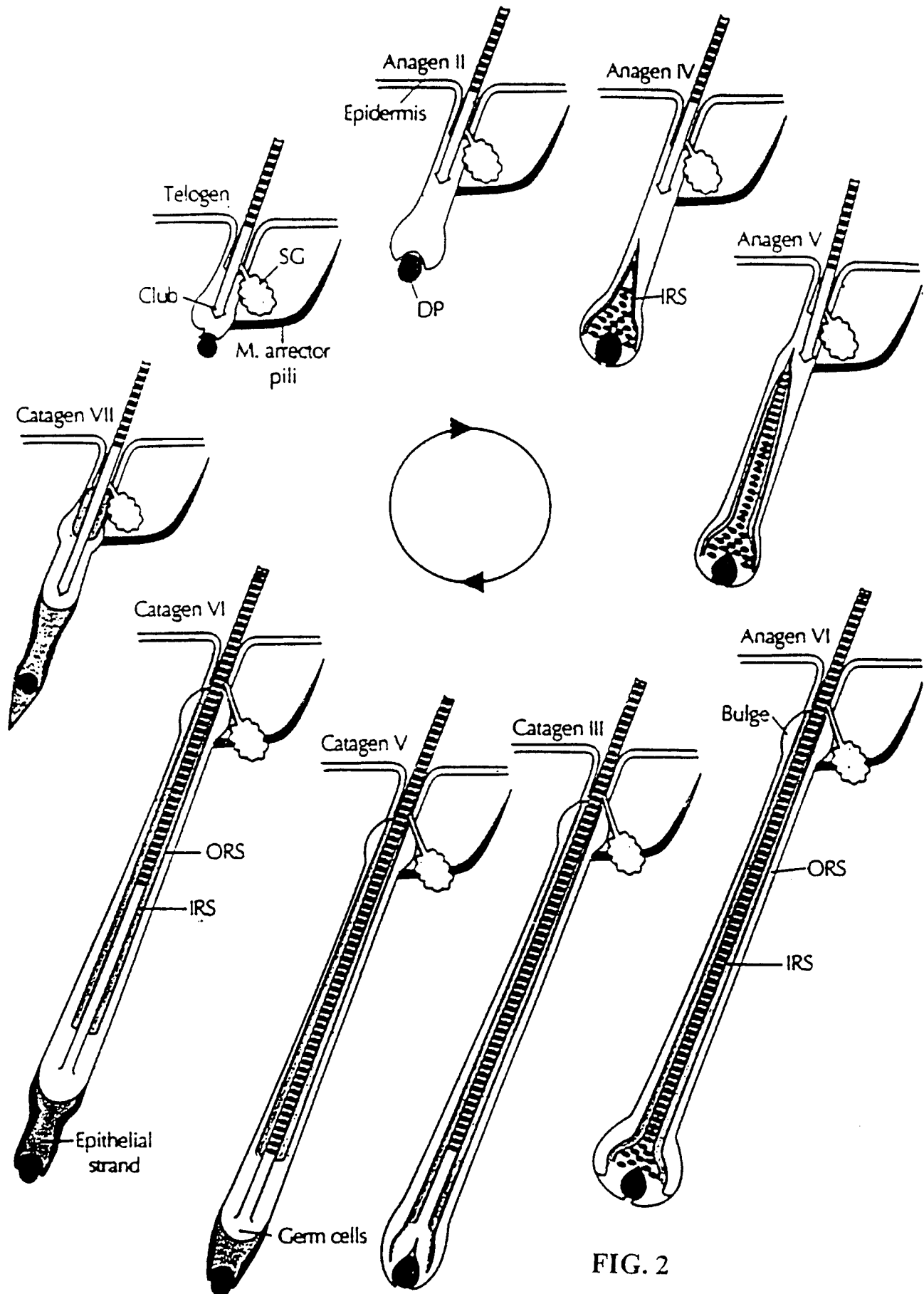


FIG. 2

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— PLUCKED HAIR FIBRE MORPHOLOGIES:-

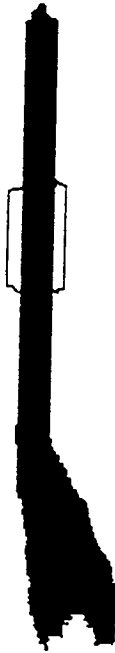


FIG. 3



FIG. 4

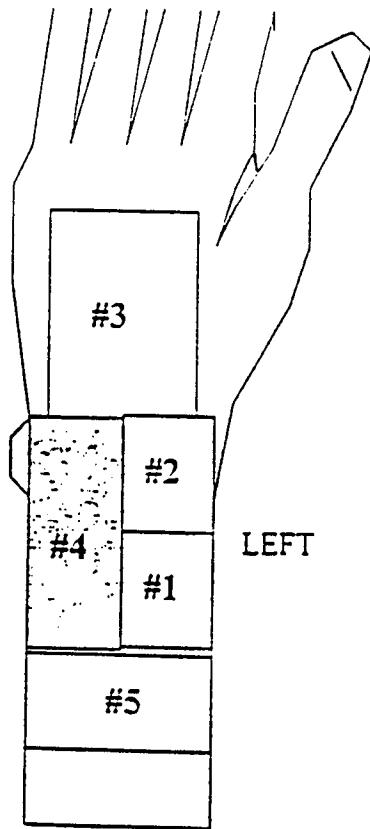


FIG. 5

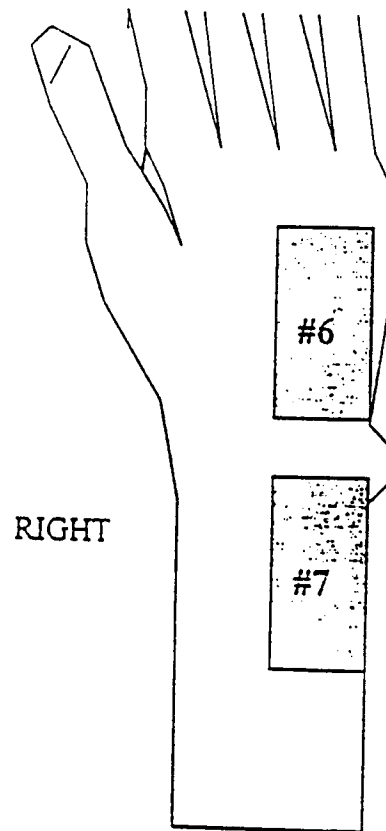


FIG. 6

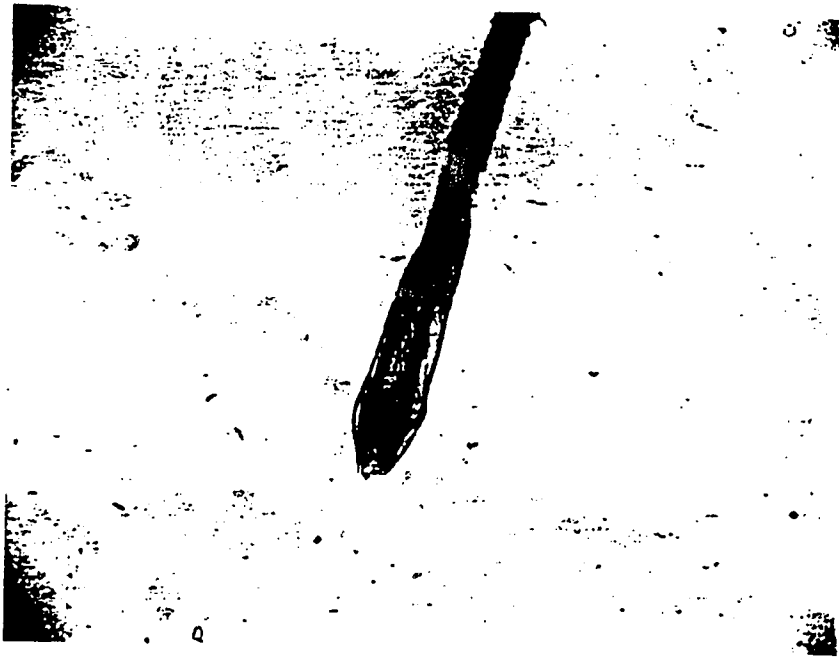


FIG. 7

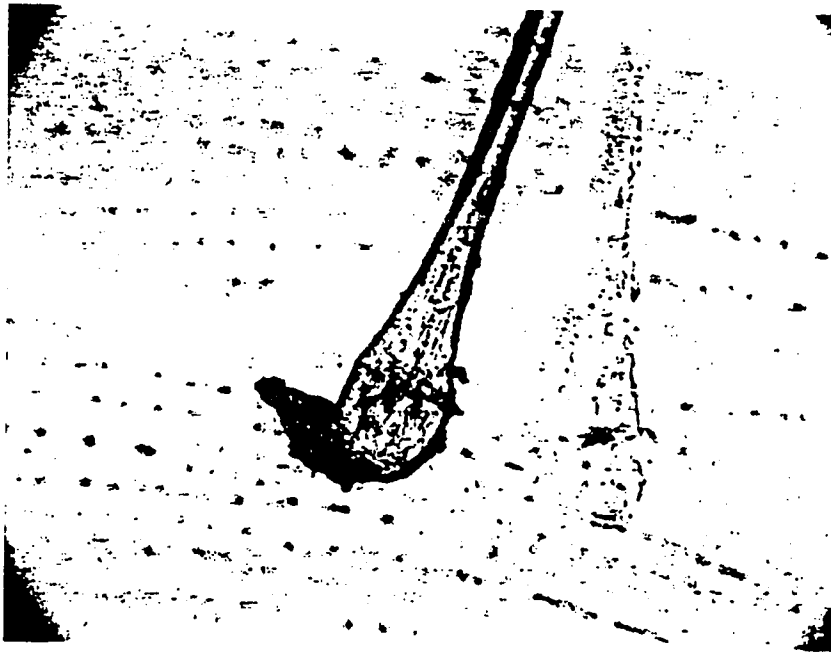


FIG. 8

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Average hair length above and below skin surface measured on the control and lased sites

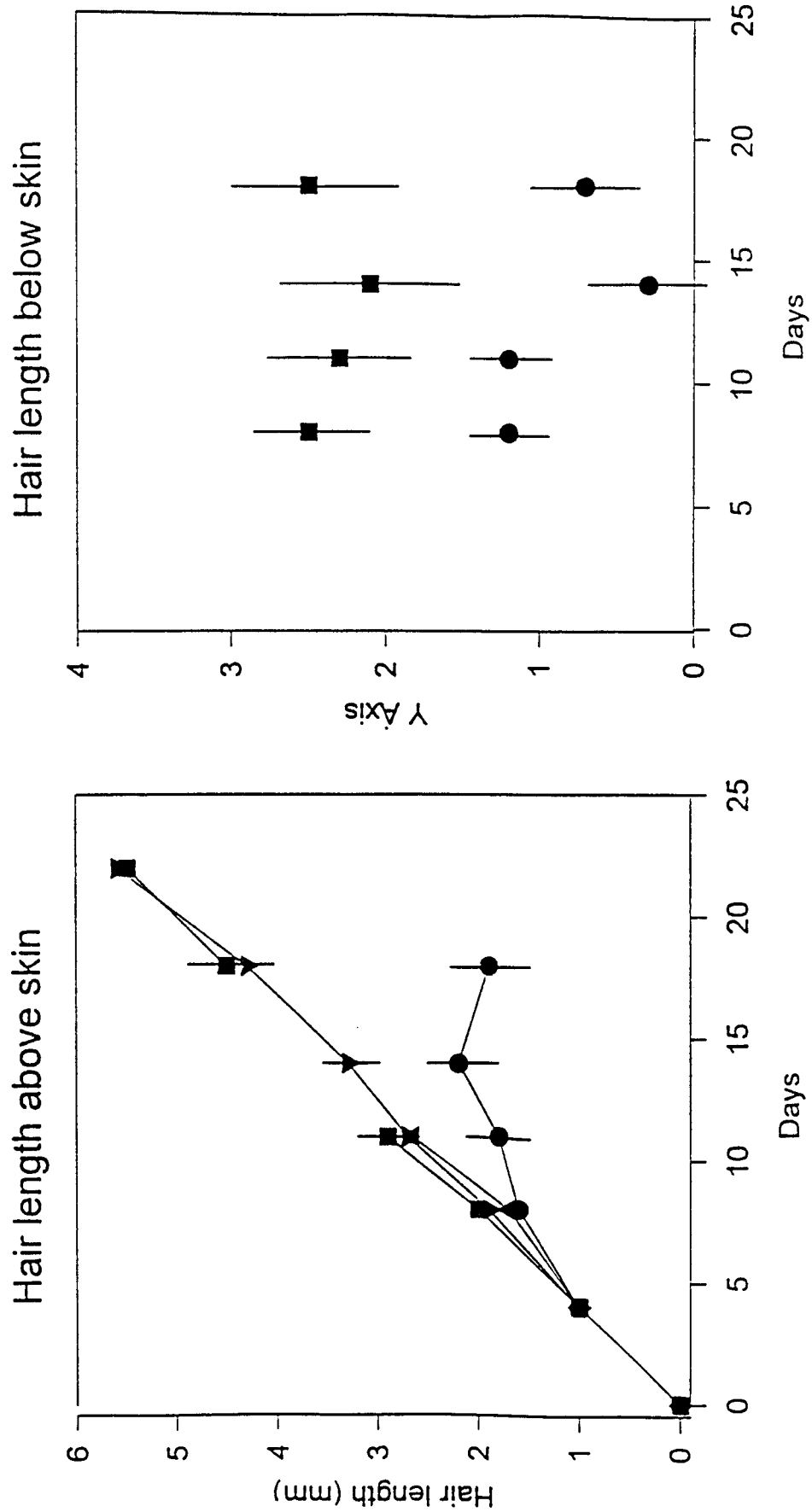


FIG. 9

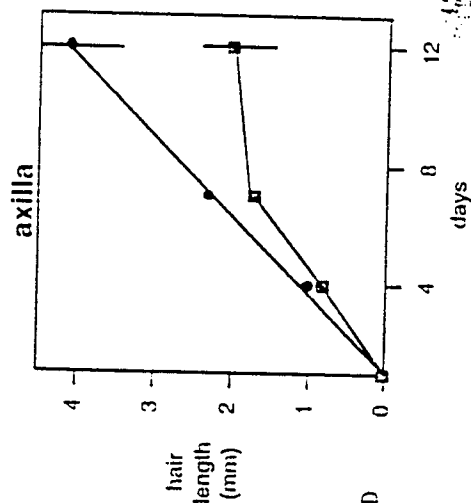
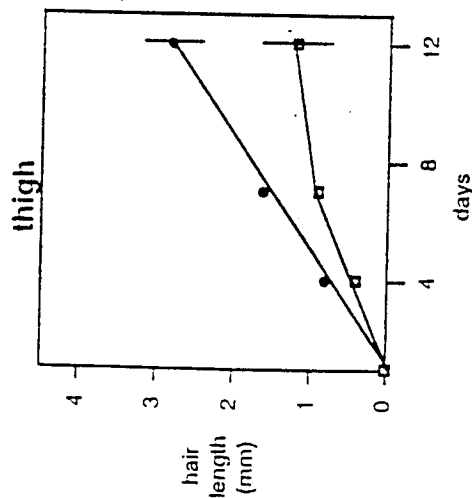
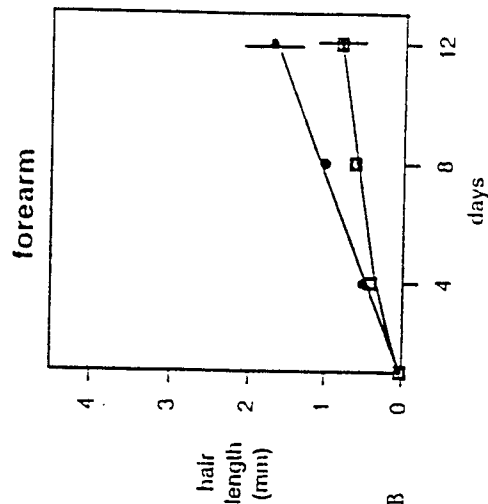
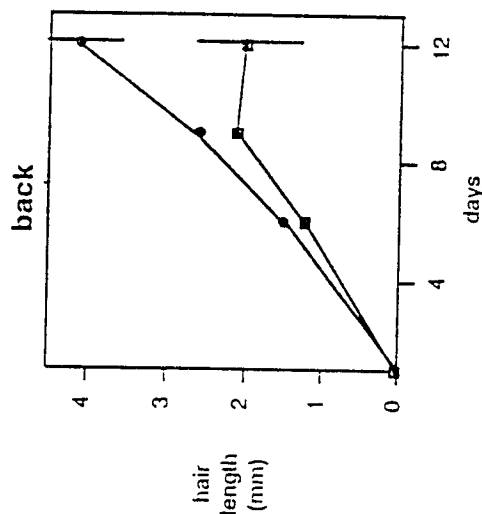
FIG. 10

file: length.spw

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Average Length of the Hair Above Skin Surface vs. Time After Laser Treatment Without Waxing

THERMO LASE
CORPORATION



• not lased
■ lased

3832-V/8-31

COOLIGHT

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Average Length of the Hair Below Skin Surface vs. Time After Laser Treatment

THERMOBLAZE
... ..

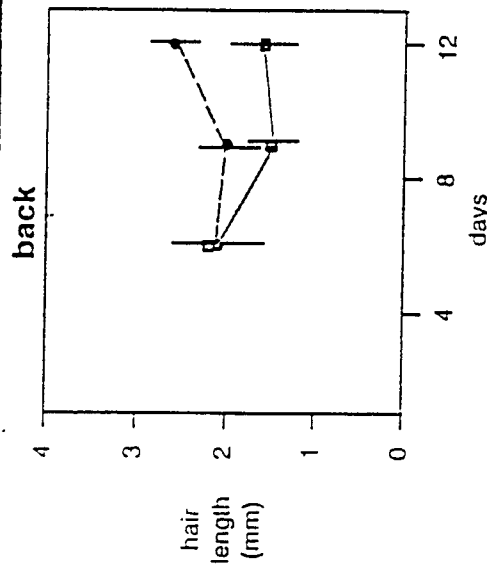


Fig. 12a

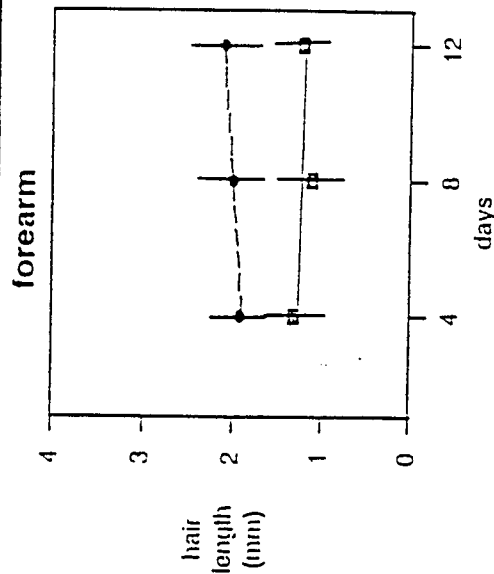


Fig. 12b

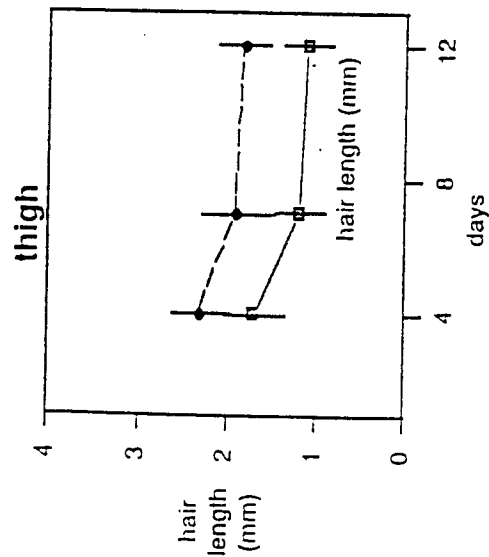


Fig. 12c

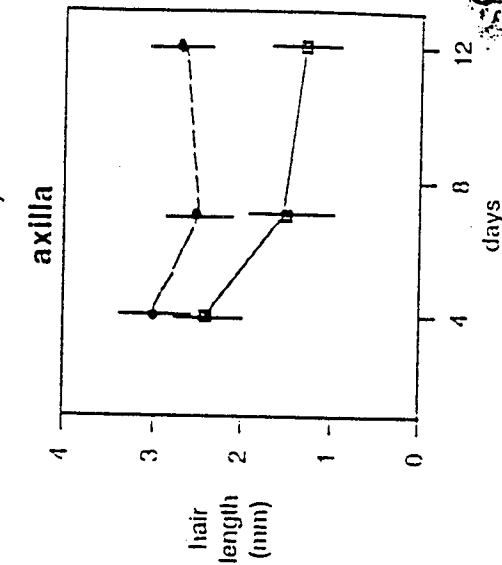


Fig. 12d

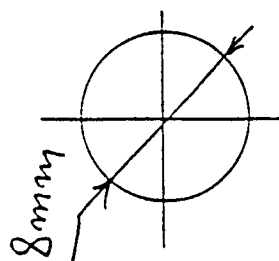
• not lased
 ■ lased

3832-V/8-32

Fig. 12

INTELLIGENT

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No reflector

Fluence rate in the incident beam = 1 J/cm^2
 Energy in a pulse = 0.5 Joule

Fluence profile in r-z plane

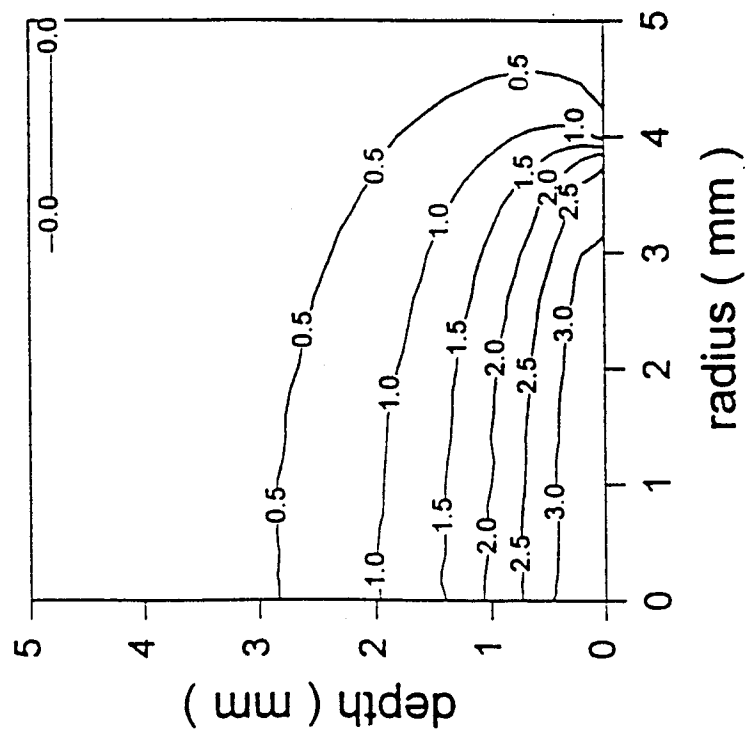


FIG. 13

Fluence in skin vs depth

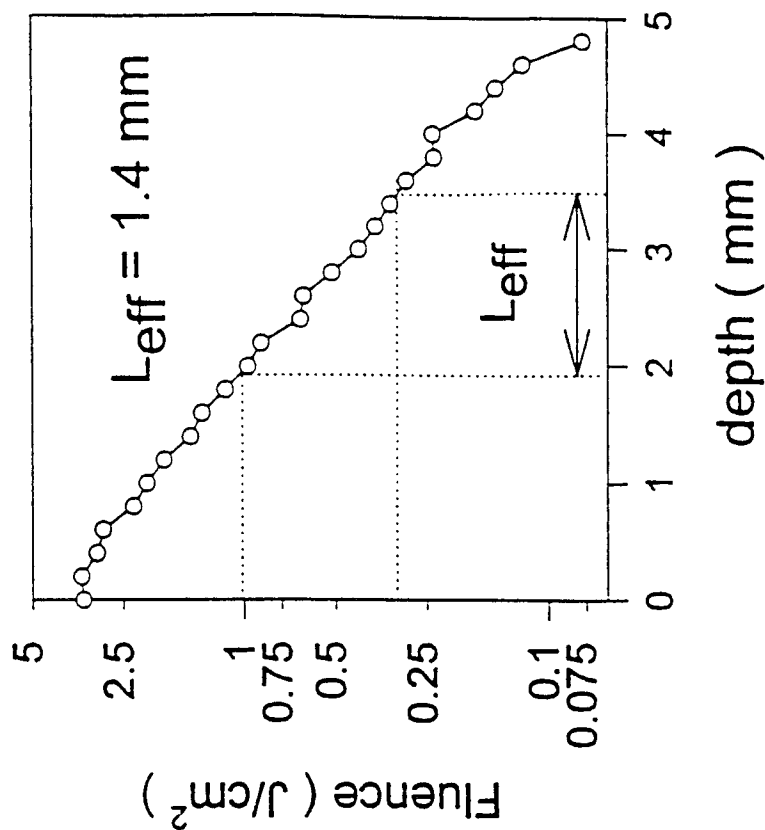


FIG. 14

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Laser beam broadening with depth in skin model#2

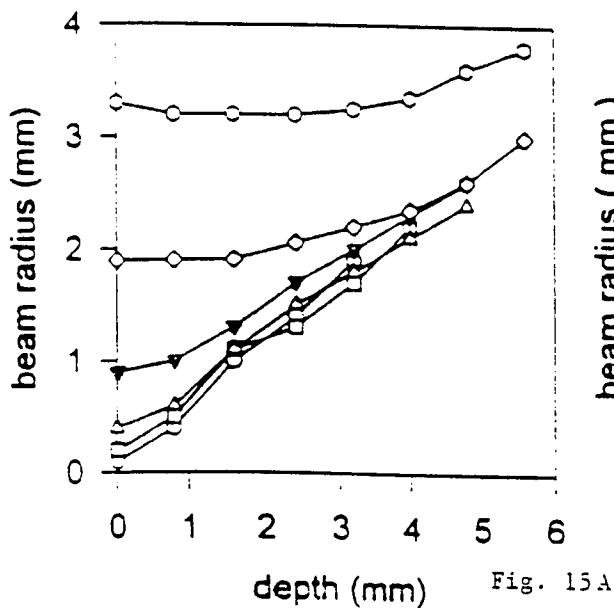
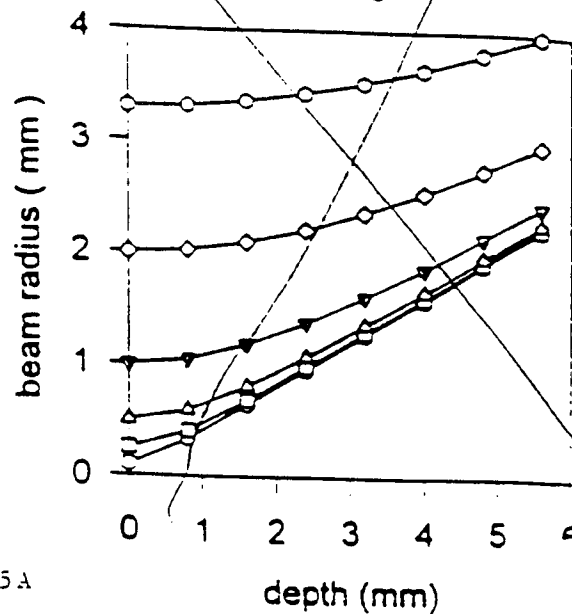


Fig. 15 A

Approximation $R(z) = \sqrt{R_0^2 + 0.16 \cdot z^2}$



Fluence in the center of laser beam vs depth for various incident beam diam

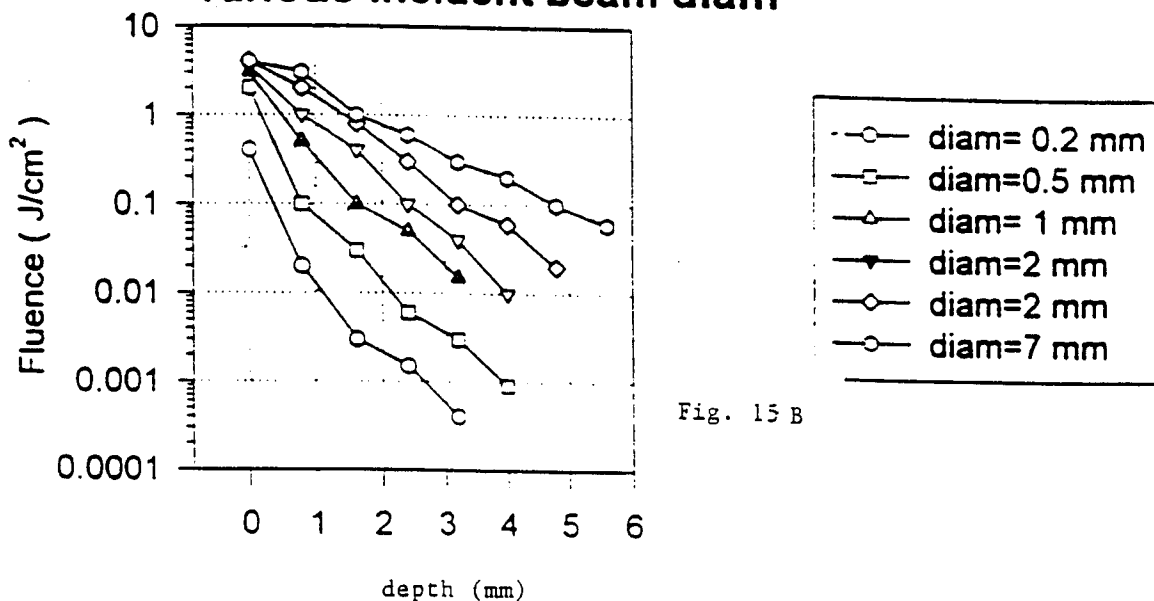


Fig. 15 B

THERMOLASE PROPRIETARY INFORMATION

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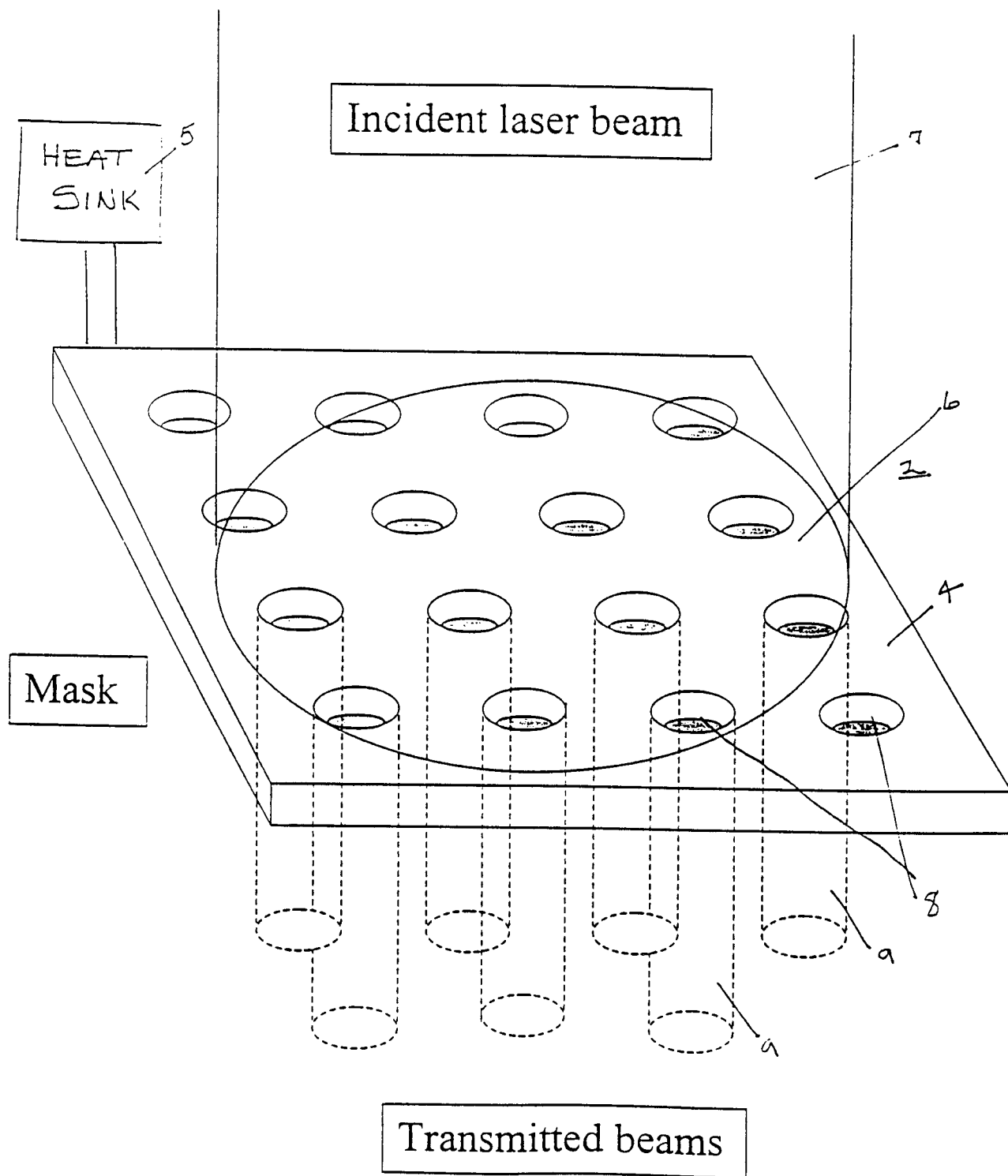
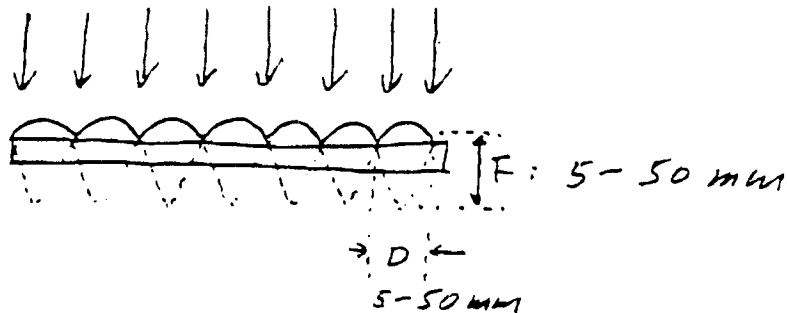
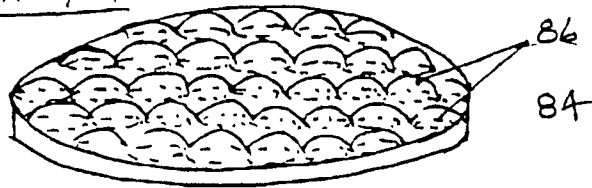


Fig. 16.A

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Array of lens for focusing down laser beam to array of small laser spots for laser therapeutics



F : focal length of individual lens

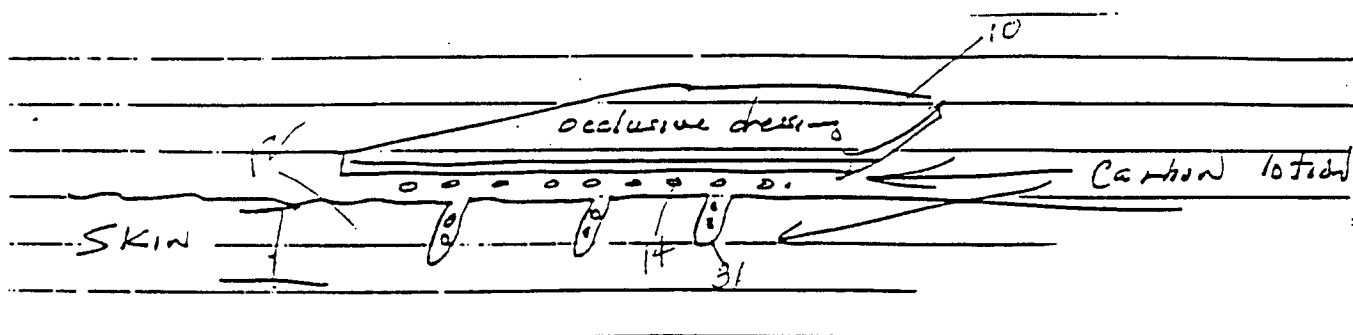
D : diameter of individual lens

Semi-sphere bumps, could be disposed in either direction relative to skin surface

Sheng Guan Shan
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Fig. 16 B

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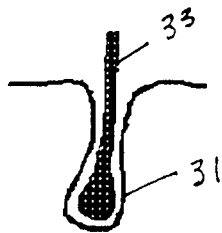


FIGURE 18A Schematic representation of hair and follicle

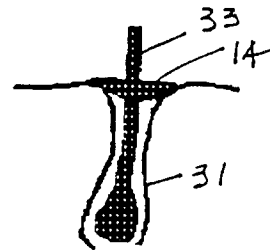


Figure 18B Photoreceptive lotion applied.

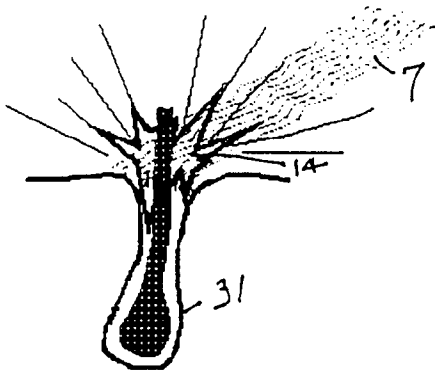


Figure 18C Upon laser irradiation, forces are not directed into follicle; Inertial and fluid effects prevent delivery of lotion.

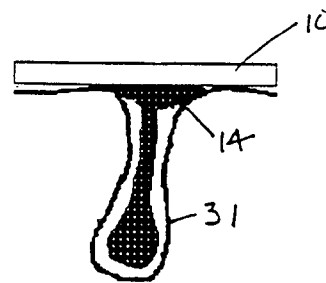


Figure 18D Hydrogel barrier applied upon skin, over lotion.

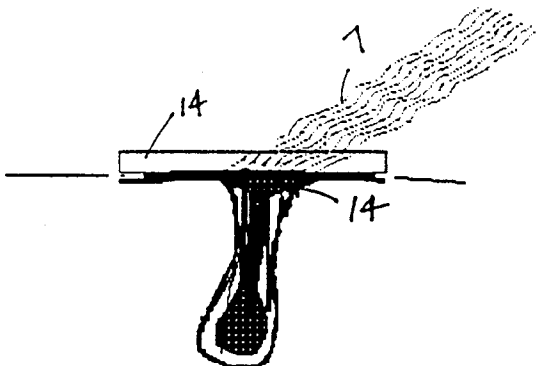


Figure 18E Upon irradiation, pressures and shock are directing lotion into follicle around hair.

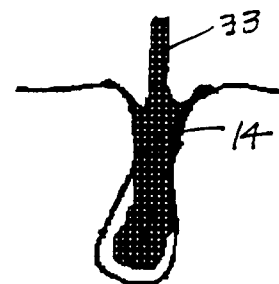


Figure 18F Lotion delivered into follicle structure.

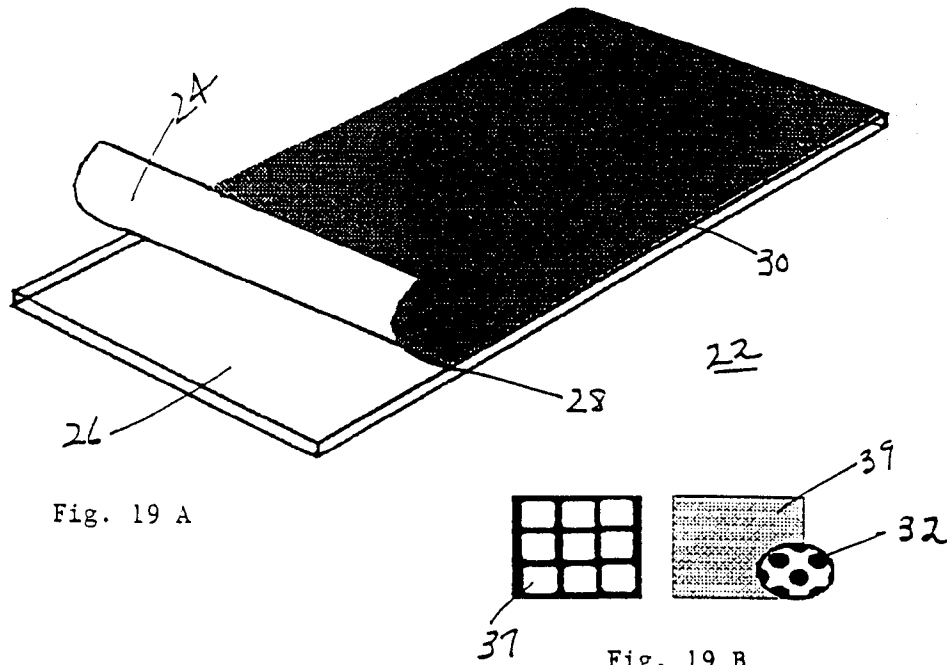


Fig. 19 A

Fig. 19 B

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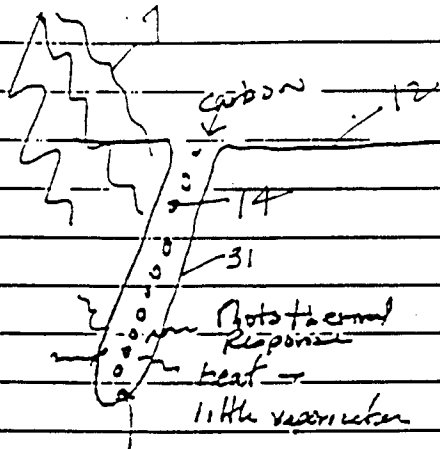
Nd:YAG
laser

Fig. 20A

laser

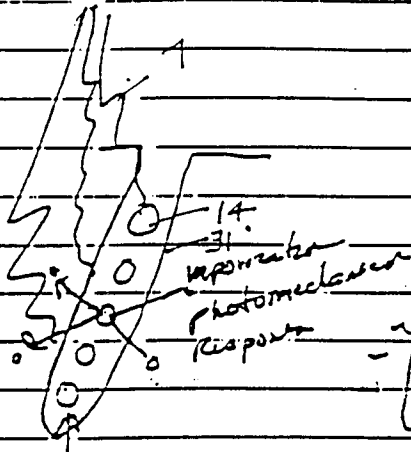


Fig. 20B

laser

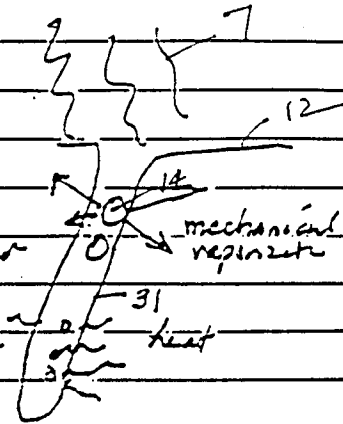
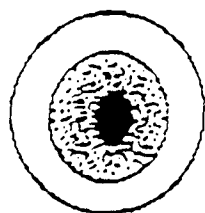
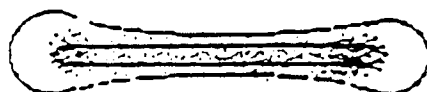


Fig. 20C



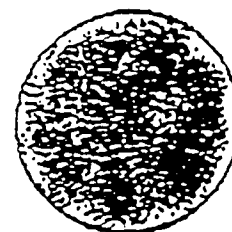
Multilayer Liposome

Fig. 21 A



Erythrocyte Shadow
with medication inside

Fig. 21B



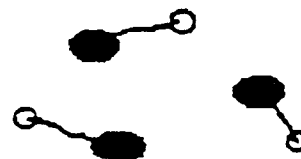
Coscarvate Drop

Fig. 21C



Latex Sphere with Monoclonal Antibodies

Fig. 21 D



Crystal particles with Drug Molecule Bound

Fig. 21E

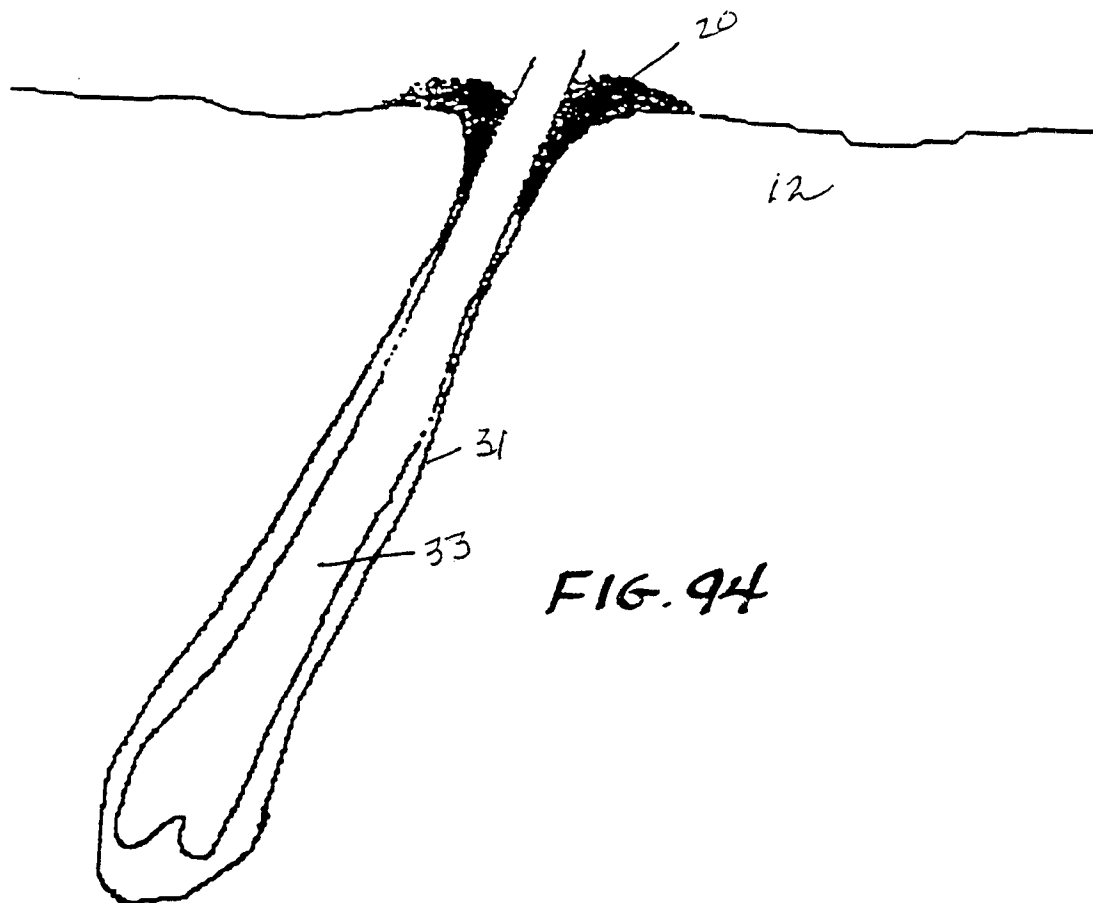


Fig. 22

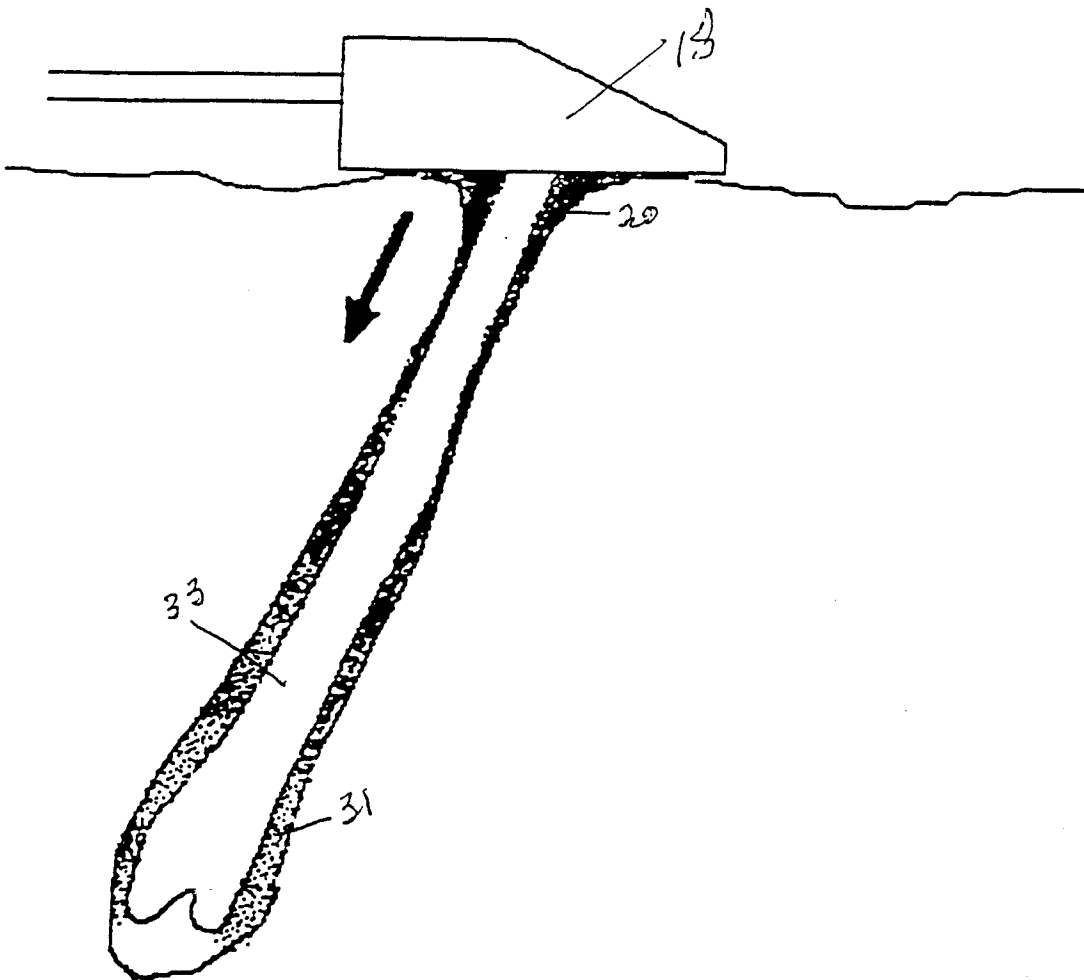


Fig. 23

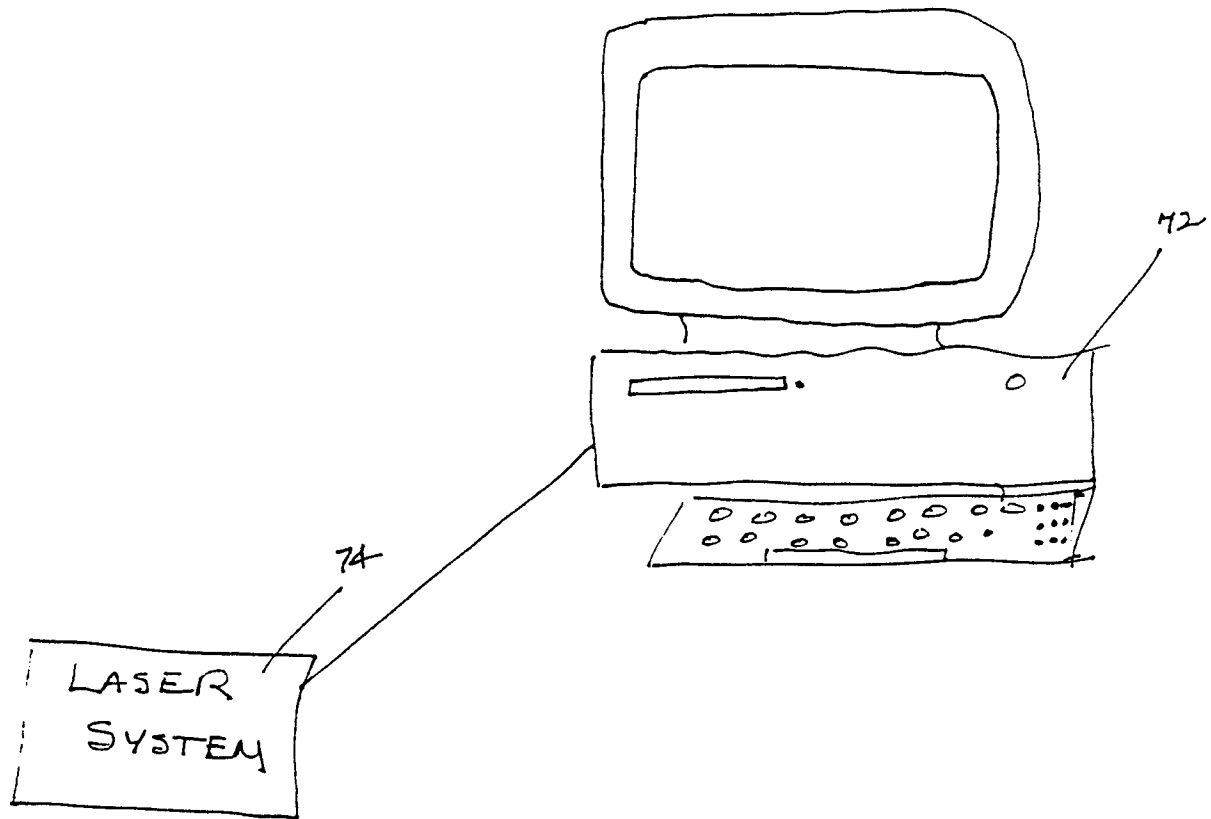


FIG. 24

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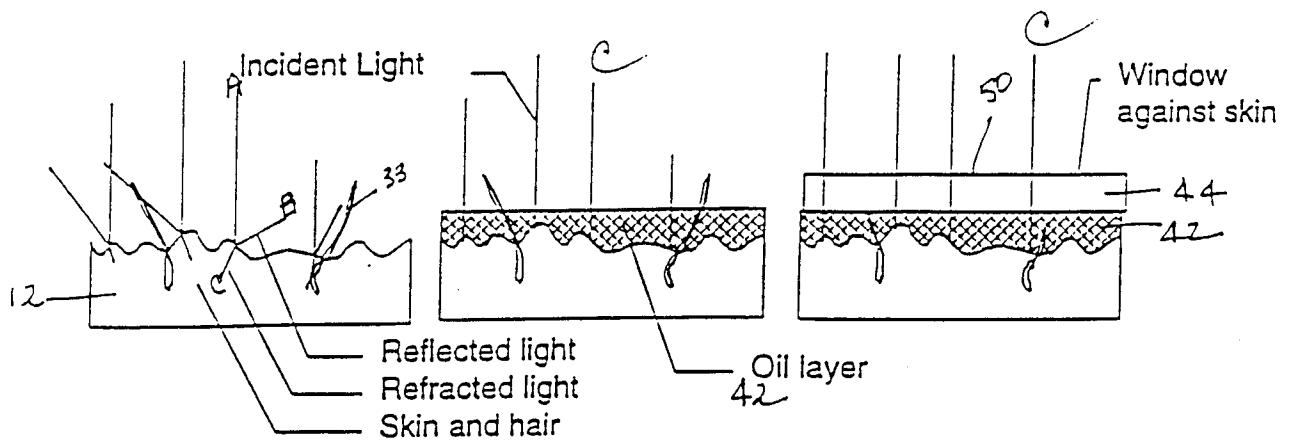


Fig. 25A

Fig. 25B

Fig. 25C

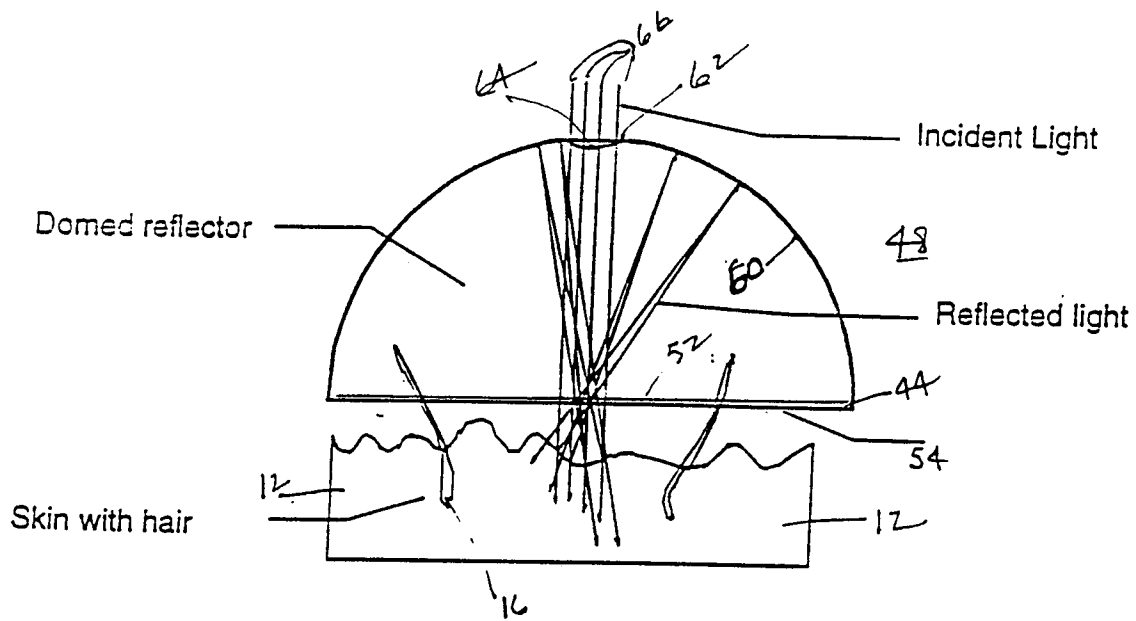


Fig. 26

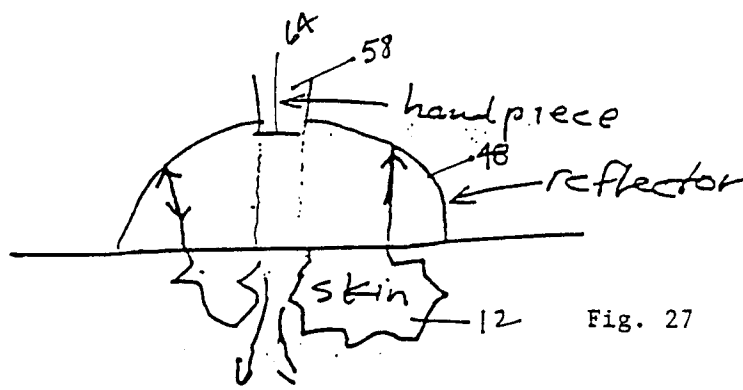


Fig. 27

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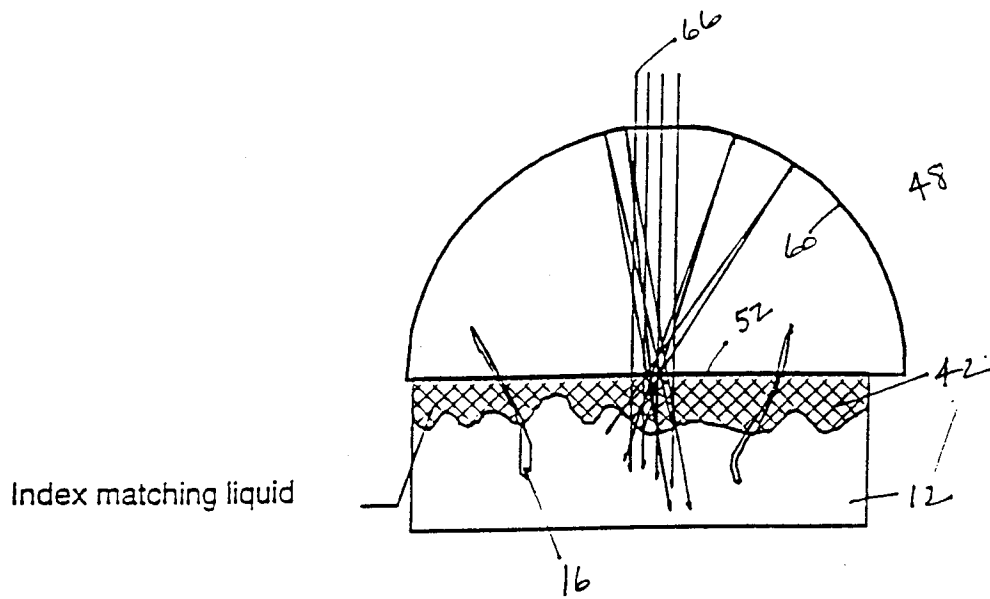


Fig. 28

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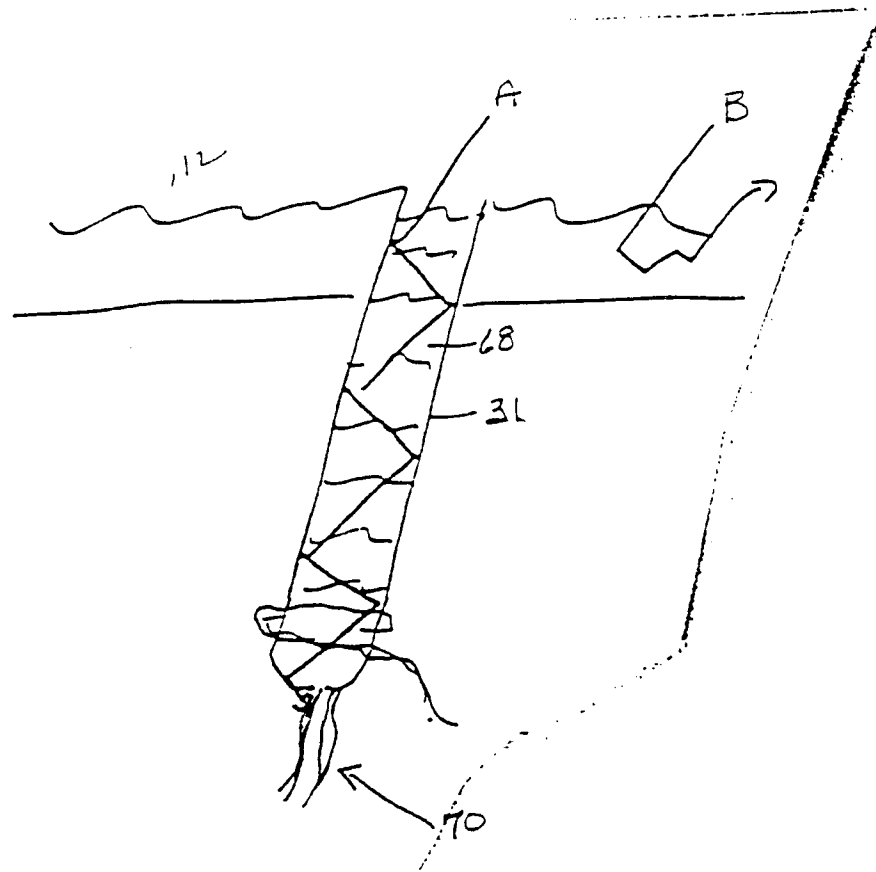


Fig. 29

Fig. 30 A

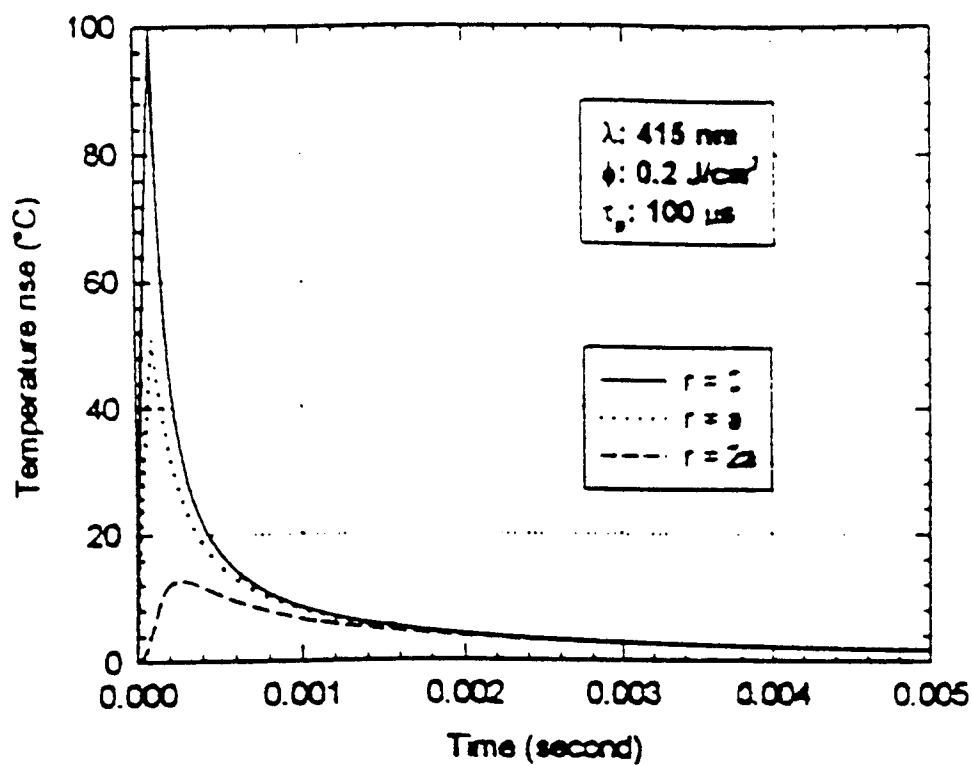
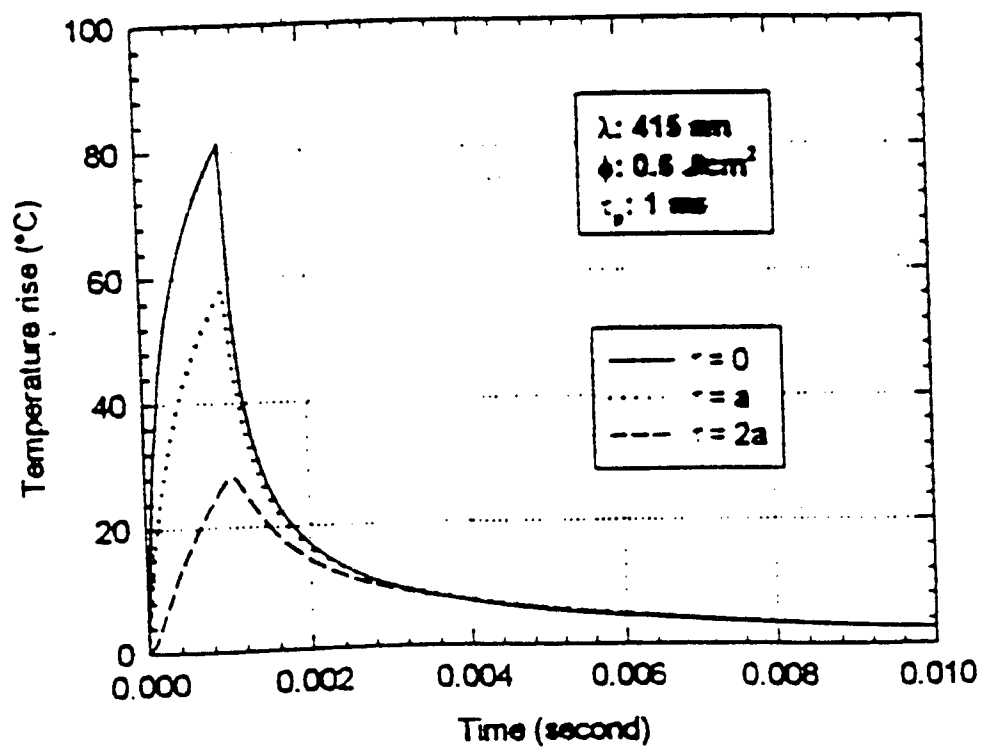


Fig. 30 B



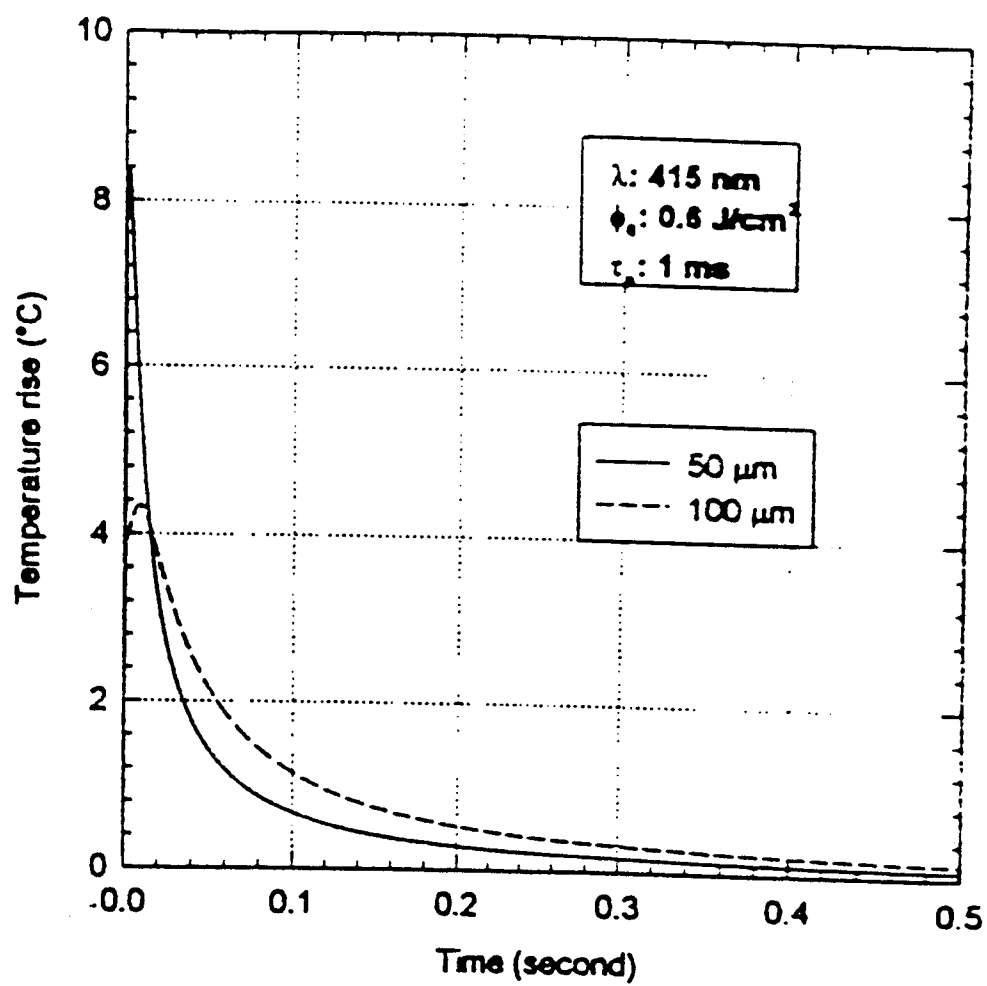


Fig. 31

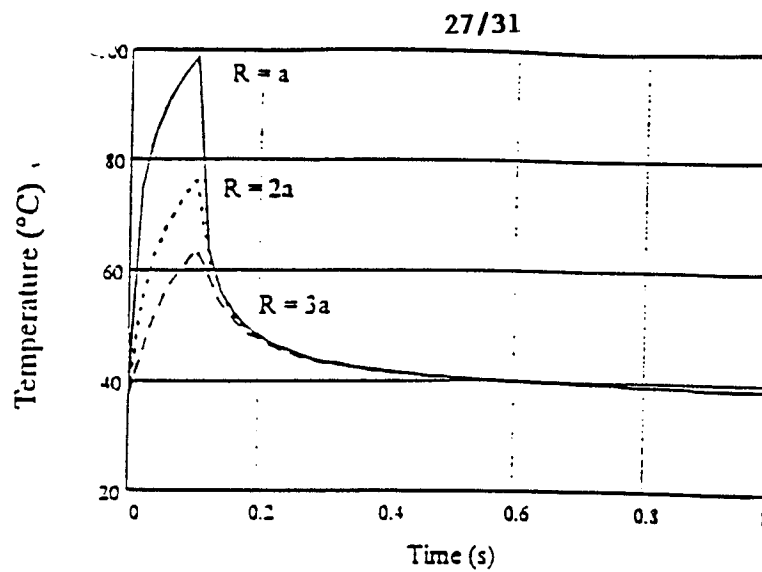


Fig. 32 Heating up of the tissue surrounding a hair follicle by laser irradiation.

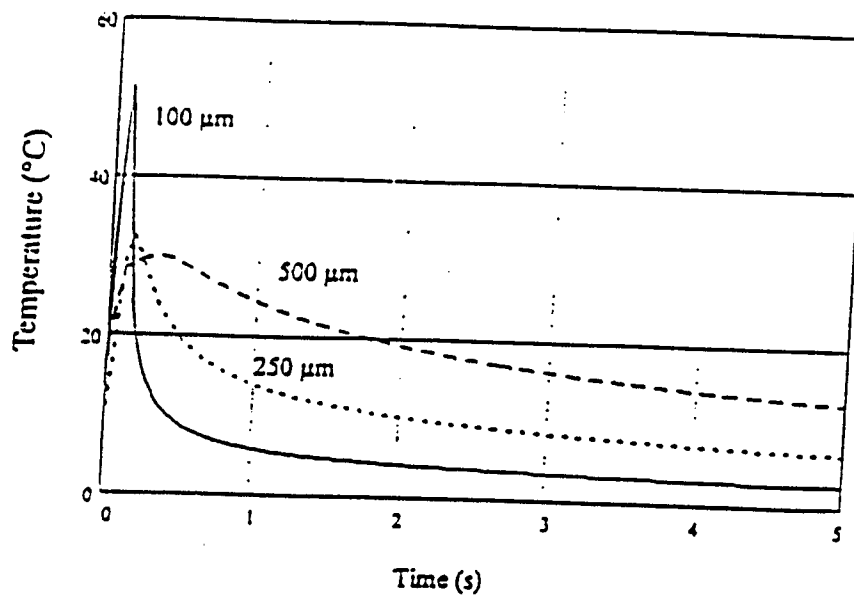


Fig. 33 The skin temperature at different depth with laser illumination and cooling of skin surface.

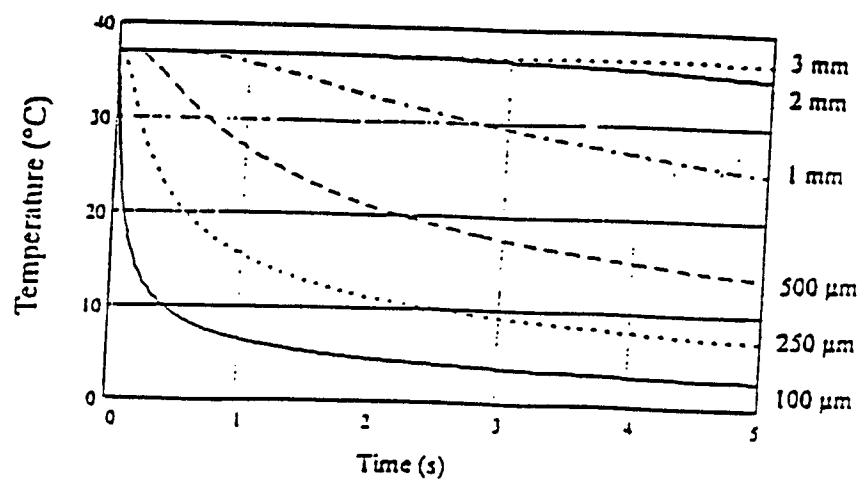


Fig. 34 The temperature of skin at different depth after its surface is contacted with a coolant at 0 °C.

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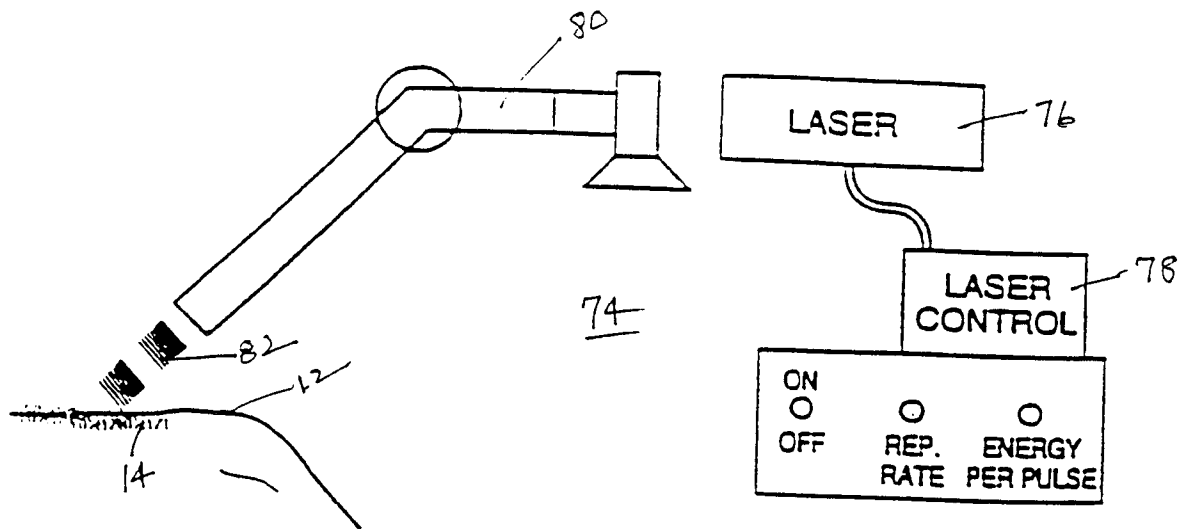
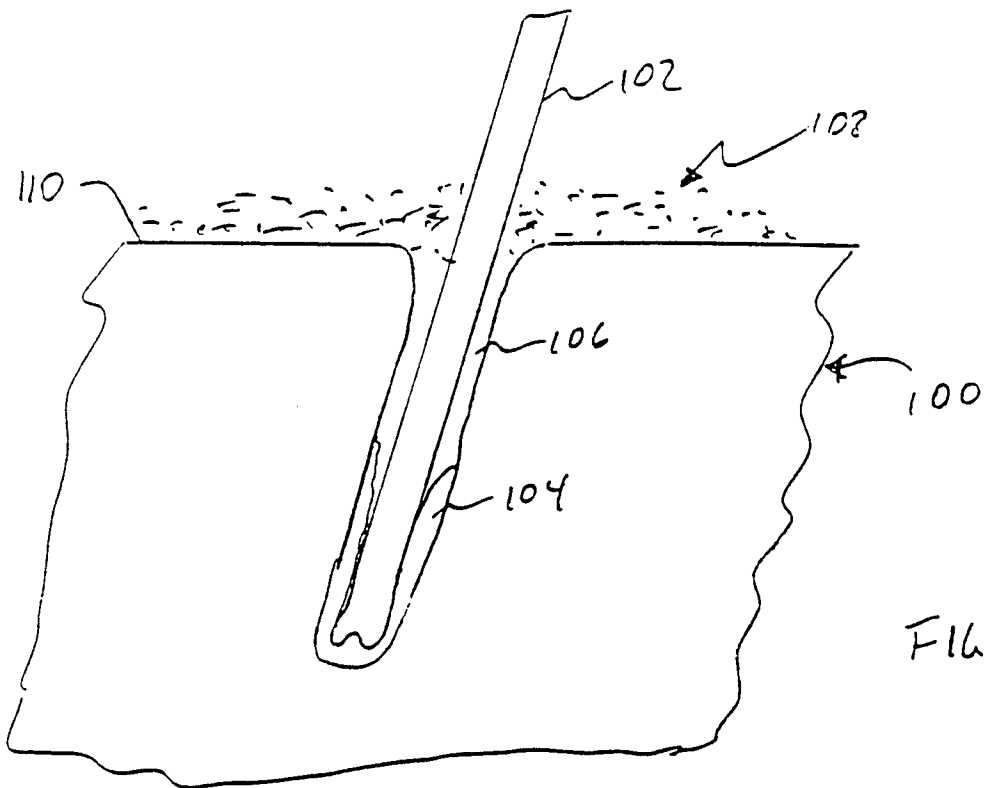
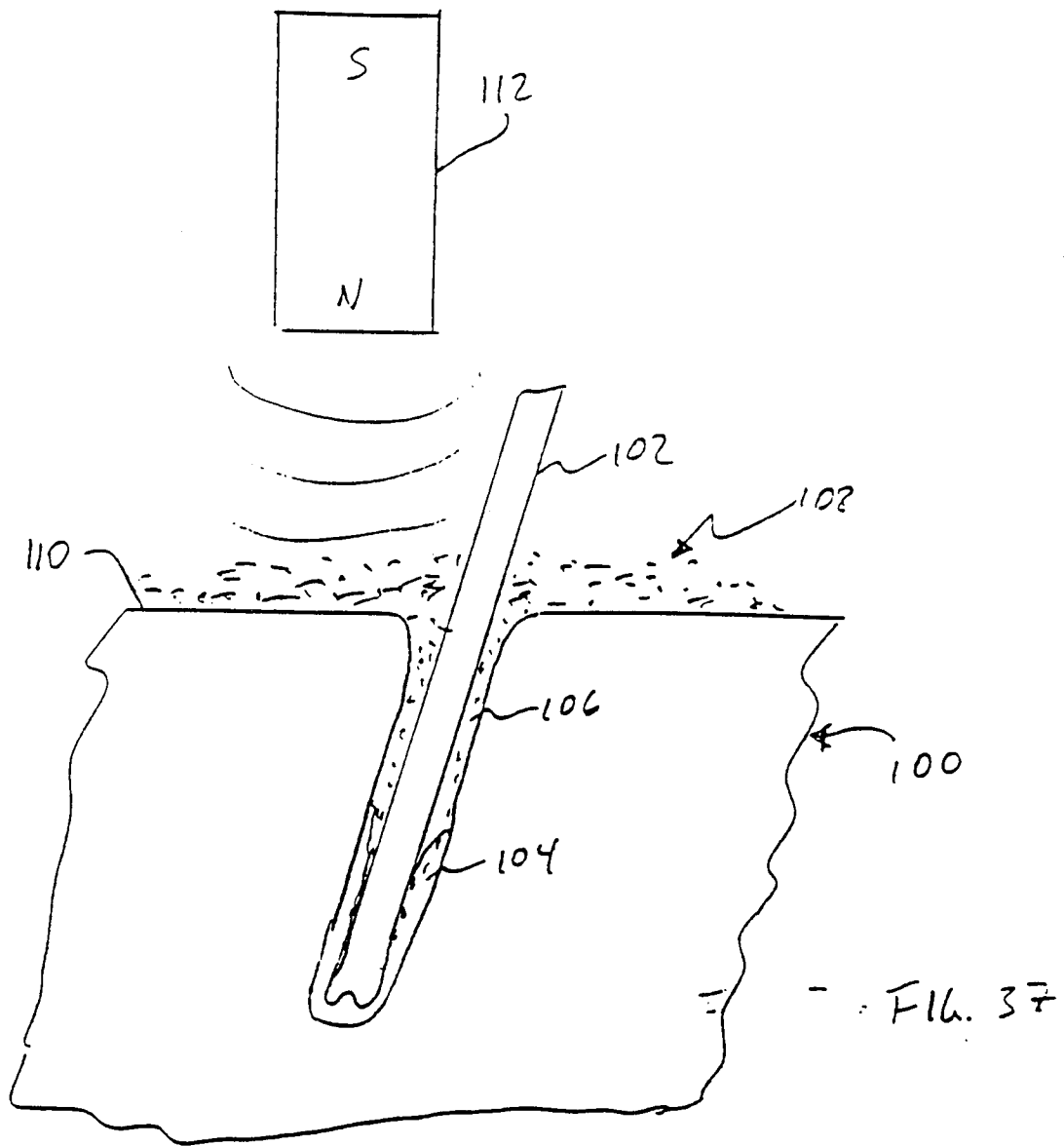
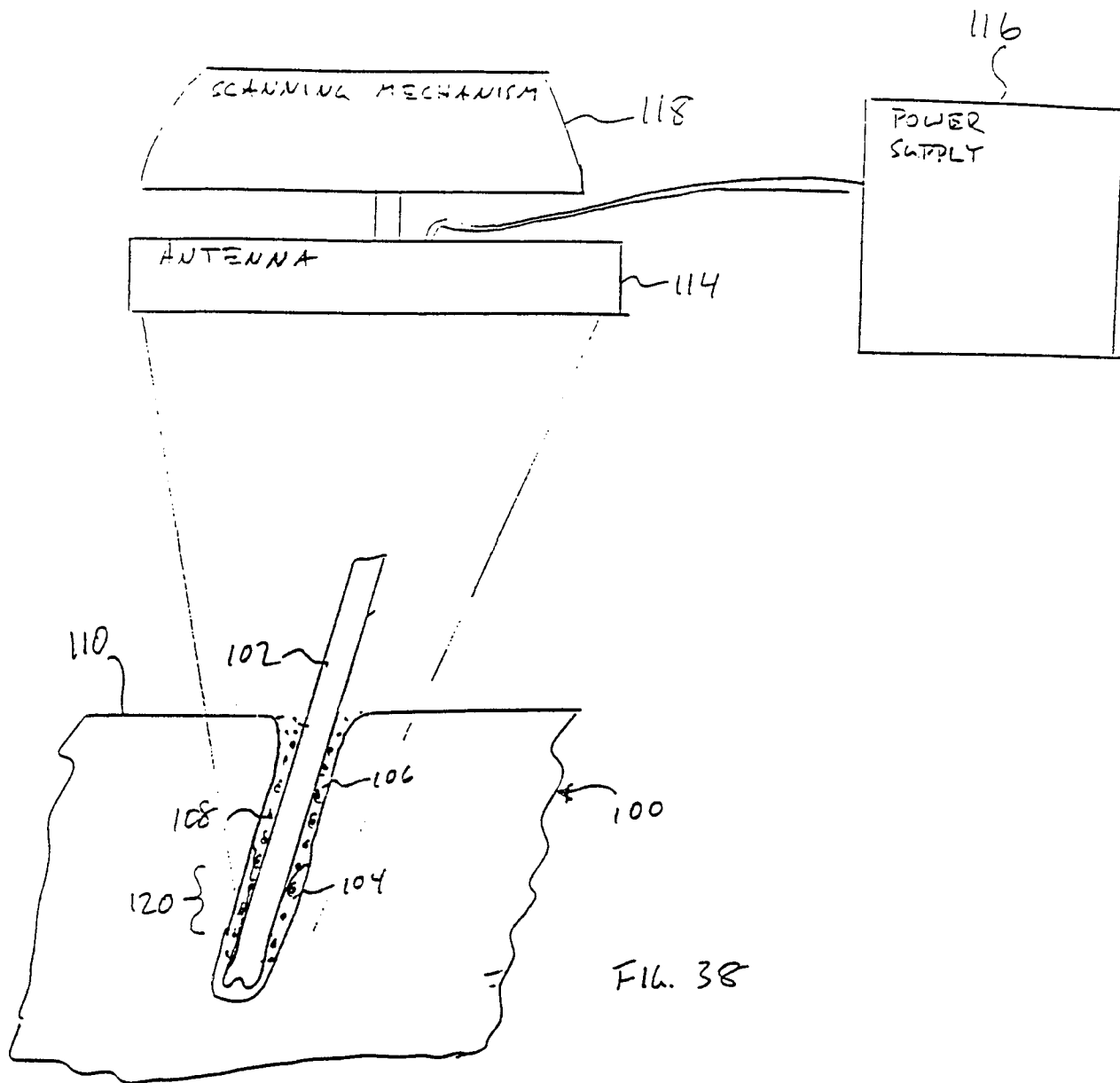


FIG. 35



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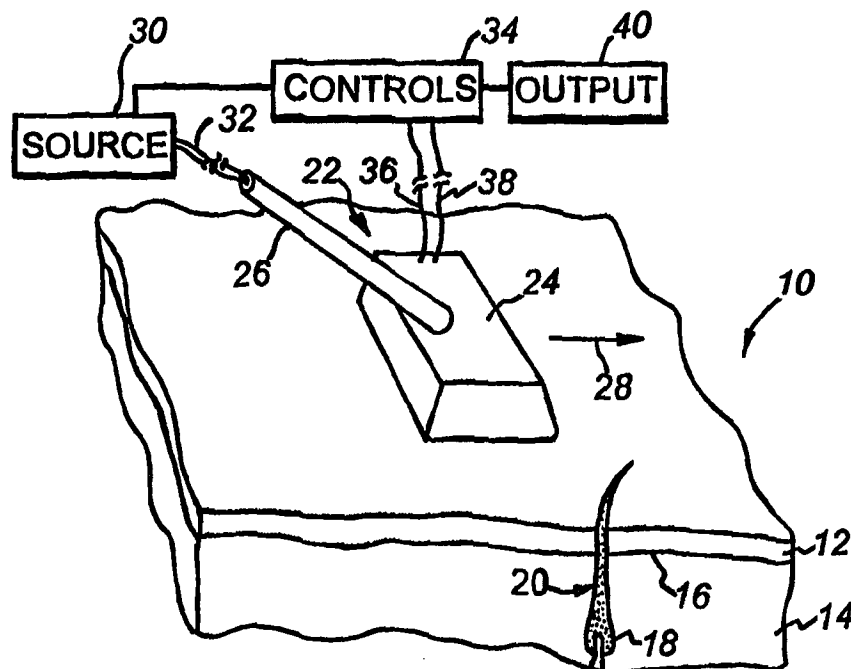


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(54) Title: METHOD AND APPARATUS FOR DERMATOLOGY TREATMENT**(57) Abstract**

Methods and apparatus for dermatology treatment are provided which involve the use of continuous wave (CW) radiation, preheating of the treatment volume, precooling, cooling during treatment and post-treatment cooling of the epidermis above the treatment volume, various beam focusing techniques to reduce scattering and/or other techniques for reducing the cost and/or increasing the efficacy of optical radiation for use in hair removal and other dermatological treatments. A number of embodiments are included for achieving the various objectives indicated above.



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METHOD AND APPARATUS FOR DERMATOLOGY TREATMENT

Related Applications

This application claims priority from provisional specifications 60/046542 filed May 15,
5 1997 and 60/077726 filed March 12, 1998, the subject matter of which are incorporated herein
by reference.

Field of the Invention

This invention relates to methods and apparatus for using optical radiation to treat
10 dermatological problems and, more particular, to such methods and apparatus which require
reduced energy and/or a lower cost radiation source by the use of continuous wave (CW)
radiation (as this term is hereinafter defined), heating of the treatment area prior to irradiation
and/or techniques for enhanced radiation utilization.

Background of the Invention

15 Lasers, lamps, and other sources of electromagnetic radiation, particularly in the optical
wavebands, are being increasingly utilized for various dermatological treatments and, in
particular, for the removal of unwanted hair, spider veins, leg veins, other veins or other blood
vessels which are visible through the patient's skin, lesions, port-wine stains, tattoos, and the like.
20 In performing such treatments, it is desirable that the cost for the treatment be kept as low as
possible, consistent with achieving desired results, and that risk of injury to the patient be
minimized.

Since continuous wave (CW) lasers and other CW radiation sources are typically
substantially less expensive than pulsed sources of comparable wavelength and energy, for cost
25 reasons, it would be preferable to use CW sources rather than pulsed sources for such
dermatological treatments. However, in order to avoid injury to the patient, the duration of
energy application to a given area of the patient's skin must be controlled, this generally resulting
in the more expensive pulsed light sources being used for the various dermatological treatments.

Further, since the only way to get radiation to areas where treatment is desired, which
30 areas are normally in the dermis, is to transmit the radiation to such area through the overlying
epidermis, some portion of incident radiation is absorbed in the epidermis creating the potential
for damage thereto. This is a particular problem where melanin is being targeted in the dermis,

as is for example the case for various hair removal treatments, since there is a substantial concentration of melanin in the lower portion of the epidermis at the dermal/epidermal (DE) junction. Further, the deeper in the dermis that treatment is desired, and/or the larger the element being treated, the more energy must be used, this generally involving the use of a more powerful laser or other radiation source and/or operating such source for longer time durations. This further increases the potential for epidermal damage.

Some attempts have been made in the past to scan a CW radiation source, such as the laser, over a treatment area, which has been done with the radiation source spaced from the skin in order to facilitate movement of the source. However, techniques currently utilized for protecting the epidermis frequently involve contact cooling of the epidermis and, for certain treatments such as hair removal, performing the treatment with pressure applied to the patient's skin is also desirable. Irradiation by use of a head in contact with the skin also permits more efficient transfer of energy into the patient's skin, thereby reducing the size of the source required for a given treatment energy density and, therefore, reducing the cost of such source. This cost could be further reduced if the radiation source is not the only source being utilized to heat the area under treatment.

Another problem in performing laser dermatology treatments, particularly when such treatment is to be performed over an area larger than the optical aperture of the applicator being utilized, is to obtain substantially uniform irradiation over the area so that sufficient radiation is applied to all portions of the area to achieve the desired treatment, while no portion of the area has so much radiation applied thereto as to cause thermal damage to the skin. Such uniform irradiation is very difficult with a pulsed source which typically utilize a circular aperture. Typically, the procedure followed is to irradiate a spot with a given pulse and to then reposition the head to an adjacent spot for irradiation. If the spots do not overlap, there will be portions of the area under treatment which do not receive radiation and, unfortunately, the radiation output is frequently not uniform over the entire optical aperture, being greater near the center, and less at the edges. Therefore, there is generally some overlap between adjacent spots. However, this results in some portions of the area under treatment receiving at least a double dose of radiation, which poses a potential danger of thermal damage in these overlap areas. Substantially uniform irradiation of a treatment area is therefore virtually impossible with a pulsed radiation source utilizing existing techniques.

Another problem which increases the energy required from the radiation source utilized is that, for existing systems, heating of the target to achieve the desired therapeutic effect is accomplished solely by radiation from the radiation source. If the temperature of the target could be increased by some type of preheating of the target volume, the amount of energy required from the radiation source to complete the job would be substantially reduced. However, such preheating must be achieved in a way such that the cost of such preheating is not greater than the savings achieved by reduced requirements on the radiation source.

A need therefore exists for an improved method and apparatus for utilizing radiation, and in particular optical radiation, to treat various dermatological conditions, which technique reduces costs and enhances safety by permitting a CW rather than pulsed sources to be utilized, by providing substantially uniform irradiation of an area under treatment, which area is larger than the optical aperture of the radiation applicator being utilized, by providing a means other than the radiation source to at least partially heat the area under treatment so as to reduce the energy required from the radiation source to achieve the desired treatment, and/or by permitting contact cooling/preheating for both enhanced epidermal protection and enhanced energy transfer to further reduce source costs.

SUMMARY OF INVENTION

In accordance with the above, this invention provides a method and apparatus for effecting a selected dermatological treatment in an area of a patient's skin which involves placing a head having at least one optically transparent channel formed therethrough in contact with the patient's skin in the area under treatment. The at least one channel has a distal end in contact with a segment of the patient's skin, which segment is smaller than the area under treatment. The head is moved at a selected rate over the treatment area, which rate is preferably substantially uniform, while remaining in contact with the patient's skin and CW radiation of a wavelength appropriate for the selected dermatologic treatment is applied through the at least one channel to the patient's skin as the head moves thereover.

For preferred embodiments, at least the portion of the head in contact with the patient's skin is of a thermally conductive material and the head is utilized to control the temperature of the patient's skin in the area to be treated prior to treatment, during treatment and/or after treatment. In particular, the portion of the head which passes over the treatment area prior to irradiation may be heated so as to heat the segment of the area under treatment prior to treatment

to a temperature below that at which thermal damage to the skin occurs. Alternatively, this portion of the head may be cooled to cool the segment to be treated, or at least the epidermal layer thereof, so as to protect this layer from damage. For one embodiment of the invention, the portion of the head in front of the at least one channel through which radiation is applied to the treatment area is divided into a first portion and a second portion which are thermally insulated from each other, with the first portion being heated by a first component and the second portion being cooled by a second component. This results in the preheating of the area or volume to be treated and the cooling of the epidermis above such treatment area prior to treatment. Either the optical channel itself, or the area around, it may also be cooled so as to cool the patient's epidermis during irradiation, and the portion of the head trailing the at least one optical channel may also be cooled to further protect the epidermis.

The apparatus may include a handle projecting from the head which handle is suitable for use by an operator to move the head over the area and an indicator of the rate of head movement. The optically transparent channel may be a single elongated channel having a waveguide or lens extending at least part way through the channel and projecting from the bottom of the head. For at least one embodiment of the invention, this waveguide is cooled during treatment. Alternatively, the at least one optically transparent channel may include a plurality of first optical waveguide elements angled at a first angle and a plurality of second optical waveguide elements angled at a second angle, with the first and second angles being selected so that light passing through the first and second optical waveguide elements converge at a selected depth, which depth is preferably at the depth in the area under treatment at which the dermatologic treatment is to occur (also sometimes referred to as the target volume or target). For some embodiments of the invention, a recess is formed in a surface of the head in contact with the patient's skin which recess is at the distal end of the optical waveguide elements. For this embodiment, the selected depth or target is preferably at a selected location in the recess, and some means is provided for moving skin in the area under treatment into the recess as the recess passes thereover. Skin may be moved into the recess by, for example, applying negative pressure to the recess or by shaping the recess to force successive folds of skin therein as the head is moved over the area with the contacting surface of the head in pressure contact with the patient's skin. For an embodiment where the apparatus is a hair-removal apparatus, the recess may be sized so as to normally receive a fold of the patient's skin which contains one or more hair follicles situated along a line generally perpendicular to the direction of movement.

For another embodiment of the invention, the transparent channel includes a cylindrical lens, which cylindrical lens may be stationary or may be mounted so as to rotate as the head is moved over the area. The head may also include a mechanism for measuring the rate at which the head is being moved over the treatment area and controls responsive to such mechanism for determining if the head is moving over the area at a rate within a predetermined range. The measuring mechanism may for example be optical or kinematic. Thermal, electronic and magnetic measuring mechanisms can also be used. The controls may provide a selected output in response to a determination that the head is moving at a rate outside of the desired range, for example, an audio or visual indication to the operator, so that the operator may adjust the rate of movement of the head to be within the desired range. In the event that the head is being mechanically driven over the treatment area, the output from the controls could function as a feedback control to the drive mechanism. The controls could also be responsive to the measuring mechanism for determining if the head is moving at a rate which poses a danger of injury to the patient, application of radiation through the at least one channel to the patient's skin being terminated in response to a danger-of-injury indication.

The rate at which the head moves over the treatment area determines the dwell time of the radiant energy on each segment of the patient's skin. This rate should be fast enough to prevent thermal damage to the patient's skin, but slow enough so that the skin segment under treatment receives sufficient radiation to achieve the desired therapeutic effect. Further, for preferred embodiments, the distal end of the at least one transparent channel has an astigmatic shape, being narrower in the direction of head movement than in a direction normal thereto. This permits a relatively large area to be treated at a given time, thereby reducing the time required to treat a given treatment area, while providing reasonable control/sensitivity for dwell time on a given segment.

While for preferred embodiments, preheating of the skin in the treatment area is accomplished in conjunction with the use of CW radiation and movement of the head over the treatment area, this is not a limitation on the invention, and preheating of the treatment area is also advantageous when employed with a pulsed radiation source. For such applications, preheating could be achieved by heating the waveguide or the portion of the head in contact with the segment under treatment prior to treatment to heat the skin down to at least to the depth where treatment is desired to a temperature which temperature is below that at which thermal damage at any depth occurs; and to then cool the surface in contact with the epidermis to cool the

epidermis before irradiation begins. This results in the area under treatment having an elevated temperature when irradiation begins, thereby reducing the energy required from the radiation source. Alternatively, a low energy radiation source, which can be either the same or different than that used for treatment, can be used to perform the preheating operation.

5 The foregoing and other objects, features and advantages of the invention will be apparent in the following more particular description of preferred embodiments of the invention as illustrated in the accompanying drawings.

IN THE DRAWINGS

10 Fig. 1 is a semi-schematic perspective view of apparatus suitable for practicing the teachings of this invention;

 Fig. 2 is a sectional view of a head useful for practicing the teachings of this invention in accordance with a first embodiment;

 Fig. 3 is a sectional view of a head suitable for practicing the teachings of this invention
15 in accordance with a second embodiment;

 Fig. 4 is a sectional view of a head suitable for practicing the teachings of this invention in accordance with a third embodiment;

 Fig. 5 is a perspective sectional view of a head suitable for practicing the teachings of this invention in accordance with a fourth embodiment;

20 Figs. 6a-6b illustrate two embodiments of astigmatic transparent channel suitable for use in a head of the various embodiments to deliver radiant energy;

 Fig. 7 is a side view of a head in use which is suitable for practicing the teachings of this invention in accordance with a fifth embodiment;

 Fig. 8 is a side sectional view of a head suitable for practicing the teachings of this
25 invention in accordance with a sixth embodiment;

 Fig. 9 is a top perspective view of a head suitable for practicing the teachings of this invention in accordance with a seventh embodiment;

 Figs. 10a and 10b are a side sectional view and a front view, respectively, of a head suitable for practicing the teachings of this invention in accordance with an eighth embodiment;

30 Figs. 11a, 11b and 11c are a side view, a front view when not in contact with a patient's skin, and a front view in contact with the patient's skin, for a head suitable for practicing the teachings of this invention in accordance with a ninth embodiment;

Figs. 12a and 12b are perspective views of portions of a head illustrating various techniques for scanning a radiation source across an astigmatic radiation delivery channel;

Fig. 13 is a side sectional view of a head suitable for practicing one aspect of the invention in accordance with a tenth embodiment;

5 Fig. 14 is a graph illustrating the relationship between temperature at the basal layer and scanning velocity when practicing the teachings of this invention; and

Fig. 15 is a chart illustrating the relationship between scanning velocity of the head and the maximum temperature of a hair bulb located at a selected depth.

10 Fig. 16 is a chart illustrating the relationship between power per unit length and maximum temperature of the hair bulb at a selected depth for two different sizes of hair bulb.

DETAILED DESCRIPTION

Fig. 1 illustrates a general system suitable for practicing the teachings of this invention. In Fig. 1, an area 10 of a patient's skin is shown on which a selected dermatologic treatment is to be performed. As indicated earlier, the treatment may be for removal of unwanted hair, tattoos, port wine stains, spider veins or other vascular lesions, etc. The patient's skin has an epidermal layer 12 and a dermal layer 14, with a dermal-epidermal (D/E) junction or basal layer 16 therebetween. While some dermatologic treatments may involve heating the epidermis 17, such as for example skin resurfacing, most dermatologic treatments which involve the use of optical radiation treat a condition located at a selected volume (sometimes hereinafter referred to as the target volume or target) within dermal layer 14. For example, when the dermatological treatment is hair removal, it may be desired to heat and destroy the bulb 18 of a hair follicle 20. While epidermis 12 might for example be 0.01 cm deep, bulb 18 might, for example, be 3.0 to 5.0 millimeters into the skin. Utilizing the teachings of this invention, a plurality of hair follicles 20 may be simultaneously heated and destroyed.

The apparatus of this invention includes an applicator 22 which may be mechanically driven, but which, for purposes of the following discussion, will be assumed to be hand operated (i.e., translated over the skin surface by hand). Applicator 22 includes a head 24 in contact with the patient's skin in the treatment area and a handle 26 which may be grasped by an operator to move head 24 in for example direction 28 across the patient's skin while preferably maintaining contact between head 24 and the patient's skin. Such contact should be under sufficient pressure between the surface of the head and the skin surface so as to, for preferred embodiments, assure

good thermal and optical contact therebetween. Such pressure can be achieved by pressing the head against the skin, by using negative pressure to press the skin against the head or some combination of the two.

For some embodiments of the invention, a source of optical radiation 30 is connected to a light pipe 32, which for the embodiment of Fig. 1 is shown as extending through handle 26, but may otherwise be connected to head 24, to selectively provide optical radiation to the head, radiation being applied through the head, in a manner to be discussed later, to the patient's skin. Source 30 may be a coherent light source such as a ruby, alexandrite, or other solid laser source, a gaseous laser source, or a diode laser source, or may be an incoherent light source such as a flashlamp, fluorescent lamp, halogen lamp, or other suitable lamp. Depending on the desired treatment, the radiant energy may be at a single wavelength, with incoherent light sources being filtered to provide the desired wavelength, or over a selected band of wavelengths. In the following discussion, when it is indicated that radiation is being applied at a selected wavelength, this will mean either a single wavelength or a wavelength band, as appropriate. Source 30 in accordance with preferred embodiments of this invention is also a CW source which, for purposes of this invention shall be defined as either a light source which is producing radiation continuously or a pulsed source with a high repetition rate/frequency, and in particular which has a delay between pulses which is less than the dwell time of the head on a given segment. CW radiation is defined as radiation from either such source.

While in Fig. 1 source 30 is shown as external to head 24, for some embodiments of the invention which involve the use of a diode laser, diode laser bar or other sufficiently compact radiation source, the source may be located in head 24, with wires for controlling and energizing the source being connected through handle 26 or otherwise to the head. Controls 34 are also provided which receive certain information from head 24 over lines 36, for example information relating to rate of movement of head 24 over the patient's skin, or temperature of the epidermis and which may send control signals to the head over lines 38 as required. Lines 36 and 38 may be part of a cable which is also connected to head 24 through handle 26 or may be otherwise connected to the head. Controls 34 may also generate outputs to control the operation of source 30 and may receive information from the source. Controls 34 may also control selected output devices 40, for example a buzzer, light, vibrator or other feedback control to an operator or, depending on application, may be of other types known in the art.

Before discussing specific embodiments for head 24 and the manner in which the system of Fig. 1 may be utilized to treat various dermatological conditions in accordance with such embodiments, it should be appreciated that maintaining head 24 in good thermal and optical contact with the surface of the patient's skin during treatment while applying CW radiation from source 30, whether located external to head 24 as shown in Fig. 1 or within the head, offers a number of significant advantages when performing various dermatological treatments. First, as indicated earlier, for the same radiation source operating at comparable energy levels, a CW source is almost always substantially less expensive than a comparable pulsed source. Therefore, the ability to use a CW source results in a significant reduction in system cost. Second, if head 24 is moved across the surface of the patient's skin at a substantially uniform rate, the radiation applied to the patient's skin at each point along the path of travel of head 24 is substantially the same, something which, as indicated above, cannot easily be achieved with a pulsed radiation source. The head being in good optical contact with the patient's skin improves the efficiencies of energy transfer into the skin, further reducing the size and cost of the required energy source. Further, the head 24 being in good thermal contact with the patient's skin permits the head to be used to heat the volume in the patient's dermis at which treatment is to occur, for example the area of bulb 18 for a hair removal procedure, so as to reduce the amount of energy required from the radiation source in order to perform the desired procedure at this volume, thus further reducing the cost of such source. Good thermal contact also permits the head to be utilized to cool the patient's epidermis 12 before irradiation, during irradiation, and after irradiation, to protect the epidermis from thermal damage. Applying pressure to head 24 as it is moved across the surface of treatment area 10 also stretches the skin in the treatment area which can provide a number of advantages, including reducing the physical distance between the head and the target volume, reducing the coefficient of scattering in the skin so that more of the applied radiation reaches the target volume and, for hair removal, flattening the hair follicle so as to increase the area of the follicle exposed to radiation. All of these effects reduce the amount of radiation required from the source, thereby further reducing the cost of the system. Various techniques are available for measuring/detecting good thermal contact between a head and the patient's skin including the temperature profile detecting technique of copending application Serial No. 60/077726 filed March 12, 1998, which application is incorporated herein by reference.

Fig. 2 illustrates one exemplary embodiment for a hand piece 24A suitable for use in practicing the teachings of this invention. In the discussion of this embodiment, and in the

embodiments to follow, the same reference numerals will be used for common elements. Letter suffixes will be used for elements which are substantially the same, but differ in some particulars. Thus, the letters 24A, 24B, etc. are used for the various embodiments of handpiece 24.

Handpiece 24A has three sections, an optical channel 50 which is shown in Fig. 2 as a waveguide, a leading section 52 which passes over treatment area 10 before waveguide 50 and a trailing section 54 which passes over the treatment area after waveguide 50. Optical radiation is applied to waveguide 50 through optical fibers 32 (or fiber bundle) or other suitable optical transmission components or, as will be discussed later, laser diodes or other suitable components may be in contact with waveguide 50. Waveguide 50 may also be replaced with a lens or other suitable focusing or non-focusing optical transmission component (a waveguide, lens or other suitable focusing or non-focusing optical transmission component sometimes being collectively referred to hereinafter as an "optical channel"), which optical transmission component receives radiation from the radiation source utilized through a suitable optical transmission path. Other arrangements for getting radiation to optical channel 50 can also be employed.

Sections 52 and 54 are each formed of a metal or other material having good thermal conduction properties. Sections 52 and 54 may be formed as a single block of a single material, with optical channel 50 being formed in the block, or, where sections 52 and 54 are to have different temperature profiles, the sections may, as will be discussed later, be two separate sections of the same or different materials secured together with a layer of thermal insulation therebetween. In Fig. 2, a thermal component 56a, 56b, 56c is shown in contact with section 52, waveguide 50, and section 54, respectively. For a preferred embodiment, each of the thermal components 56 is a thermoelectric element such as a Peltier effect device; however, other mechanisms for controlling temperature known in the art, including flowing water, and flowing gas or spray at a desired temperature may be utilized for thermal components 56. In applications where sections 52 and 54 have the same temperature profile, the same thermal component may be used to control the temperature of both sections; however, particularly if thermoelectric components are used, it is preferable that a number of these components be utilized, distributed over sections 52 and 54 so as to achieve a substantially uniform temperature distribution in these sections.

Fig. 3 shows a head 24B which is substantially the same as the head 24A shown in Fig. 2 except that, in addition to sections 52 and 54, head 24B also has a section 58, ahead of section 52, with a thermal insulation layer 60 being provided between sections 52 and 58. Section 58 is

also formed of a metal or other material having good thermal conduction characteristics and a thermal element 56d, for example one or more thermoelectric or thermal resistance elements, is provided in thermal contact with section 58. As will be discussed shortly, section 58 is intended to have a different temperature profile than section 52.

5 For the embodiment of Fig. 2, section 52 may be utilized to either pre-heat or pre-cool the patient's skin in the treatment area. For a head 24 moving at a velocity V in direction 28, V sometimes also being referred to as the "scanning velocity", and for a length of section 52 in the direction of movement 28 equal to L_1 , the time T_1 during which section 52 is over a segment of the patient's skin prior to treatment, and thus the time of pre-heating or pre-cooling, is roughly
10 directly proportional to L_1 and inversely proportional to V. Thus,

$$T_1 = \frac{L_1}{V} \quad (1)$$

Since the time it takes for a temperature wave to penetrate to a depth z in the skin is,

$$T_z = \frac{z^2}{4\alpha} \quad (2)$$

where α is the skin thermal-diffusion coefficient ($\alpha \approx 1.5 \cdot 10^{-3} \text{ cm}^2/\text{s}$). Therefore if these two times (T_1 and T_z) are roughly equal, then:

$$z = \frac{\sqrt{4\alpha \cdot L_1}}{V} \quad (3)$$

15 and the desired thermal effect will reach a desired depth z during the period that section 52 overlies the skin segment. Thus, L_1 and V can be selected so as to achieve the desired thermal effect at a desired depth in the skin prior to irradiation. Since, as will be discussed shortly, V is also a factor in determining the duration of irradiation for achieving the desired therapeutic effect, L_1 may be the prime factor in determining the depth for the desired thermal effect. For pre-
20 heating, the depth z is the depth of the volume at which treatment is desired. For example, referring to Fig. 1, z might be the depth of bulb 18 of a hair follicle where the treatment is hair removal. For pre-cooling, it is generally desired to cool the entire epidermis 12 to DE junction 16. It is generally undesirable to cool significantly below the DE junction since this may

interfere with treatment by having some cooling effect on the treatment or target volume. Depending on the function section 52 is to perform and the scanning rate V , L_1 is selected so as to achieve the desired thermal effect to the desired depth z .

Fig. 3 differs from Fig. 2 in that there are two pre-temperature modifying sections 52 and 58. With this arrangement, section 58 is typically heated to pre-heat to the depth z_c of the target volume. Section 52 is cooled and is intended to subsequently cool the epidermis to roughly DE junction 16. Since heating performed by section 58 is to a greater depth than the cooling performed by section 52, L_4 is shown as being greater than L_1 in Fig. 3. The combination of sections 52 and 58 permits the target to be heated and remain heated prior to irradiation while the epidermis is protected against thermal damage by being cooled prior to irradiation.

The temperature profile at the depth z is a function of the initial temperature of the skin and of the temperature of the section 52, 58 for head 24B. The length of the segment L_1 and scanning velocity V are also factors in determining the final temperature at depth z . An estimate of skin temperature at depth z can be made using Thomson's equation as follows:

$$T(z, V, L_1) = 2 \cdot \frac{T_0 - T_1}{\sqrt{\pi}} \cdot \int_0^{\frac{z}{2\sqrt{\frac{\alpha L_1}{V}}}} e^{-\xi^2} d\xi + T_1 \quad (4)$$

where T_0 is the initial temperature of the skin, T_1 is the initial temperature of the segment which is assumed for purposes of the equation to be segment 52. For scanning velocities in the range of approximately 0.05 to 10 cm/s, and length L of approximately 0.125 cm, desired pre-heating to a temperature in the range of +40°C to +60°C or pre-cooling of -30°C to +20°C can be achieved. Typically, the epidermis would be cooled to the DE junction to a temperature in the -5°C to 0°C range. Scanning velocities up to 10 cm/s should be achievable with contact scanning, but scanning velocities in excess of 10 cm/s may be more difficult to achieve.

The embodiment of Fig. 3 complicates the determination of appropriate parameters since scanning velocity V , which is the same for all sections, must be selected so that pre-heating can be achieved to a desired depth with an L_4 of reasonable size, pre-cooling to the DE junction can be achieved with an L_1 of reasonable size, and the desired therapeutic effect can be achieved, using the radiation source with a given fluence and for a reasonably achievable value of L_2 . This is somewhat complicated by the fact that in order to heat deep layers of the skin (i.e., greater than

3 mm) the scanning velocity should not exceed approximately 0.1 to 0.2 cm/s, while for heating of subsurface layers of the skin (less than 1 mm) the scanning velocity can be up to 2 cm/s. This assumes an L_4 of approximately 5 cm or less.

Radiation passing through waveguide or other optically transparent component 50 is directed through the epidermis, which has preferably been pre-cooled to the target, which may have been pre-heated, in order to achieve the desired therapeutic effect. In determining the time during which the target is irradiated, account must be taken of the fact that, due to scattering in the patient's skin, the beam width at the target can be greater than L_2 , the width of radiation at the skin surface, by a value Δ . Value $L_2 + \Delta$ can be minimized by focusing of the beam. Thus, the exposure time T_2 of the target to CW radiation is given as,

$$T_2 = \frac{L_2 + \Delta}{V} \quad (5)$$

The target has a thermal relaxation time which is generally a function of its size and of its shape. It is generally desirable that the time T_2 be roughly equal to the thermal relaxation time of the target, assuming destruction of the target is the desired therapeutic effect, since this results in maximum heating of the target with minimal heating of surrounding tissue. In applications such as hair removal, where it has been found that some damage to a small layer of tissue surrounding the follicle facilitates permanent, or at least more permanent, hair removal, it may be desirable for the time T_2 to be slightly greater than the thermal relaxation time of the target. In any event, for a target having a size or diameter d , the critical velocity at which dwell time on the target is roughly equal to its thermal relaxation time is given by,

$$V_c = \frac{g(L_2 + \Delta)\alpha}{d^2} \quad (6)$$

where g is shape factor ($g=8, 16$ and 24 for stratified, cylindrical and spherical targets, respectively). Thus, where bulb 18 of a follicle is the target, g would be approximately 24. Assuming a maximum scanning velocity of 10 cm/s, and also assuming a depth $z \approx 3$ mm and $L_2 + \Delta$ of about 3 mm, equation (6) suggests that the process works best for stratified targets like fat layer with a thickness greater than 190 μm , cylindrical targets like a blood vessel with a diameter greater than 270 μm , and spherical targets like a hair bulb with a diameter greater than 320 μm . However, since, as discussed earlier, lower velocities would typically be employed in order to

achieve pre-heating and/or pre-cooling for section 52, 58, significantly larger minimum target volumes are required for the various shapes in a practical system. However, since V_c is only a guide, and times less than or greater than thermal relaxation time of the target may be appropriate in some treatments, treatable target sizes will also vary. Effective pre-heating of the target may also reduce the required dwell time to achieve a desired therapeutic effect.

Another concern when employing the teachings of this invention for dermatologic treatment is that the temperature rise at the target be sufficient to achieve the desired effect. Where the treatment being performed is hair removal utilizing techniques similar to those described in U.S. Patent No. 5,735,844 issued April 7, 1998, it is necessary to heat the hair bulb to a temperature of approximately 65°C to 75°C. The maximum temperature of a hair bulb undergoing irradiation is given by the following equation,

$$T_m = \frac{6\tau(d)(1 - \exp(-\frac{a}{\tau(d) \cdot V}))}{c \cdot \rho \cdot d} \cdot k(\lambda) \cdot \psi(z, \lambda) \cdot P + T_0 \quad (7)$$

where,

z is the depth of the bulb in the skin

T_0 is the initial temperature of the bulb before irradiation

a is the size of the irradiate zone inside the skin along the scanning direction at the depth z (as previously indicated $a = L_2 + \Delta$)

c and ρ are the heat-capacity and density of the bulb respectively

$k(\lambda)$ is the absorbing ability of the hair bulb and shaft defined by a concentration and a type of melanin, and depends on wavelength (is greater for dark hair and less for lighter hair)

$\psi(z, \lambda)$ is the radiance inside the skin at the depth z , caused by a light flux of unit power per length. It depends on both scattering and absorption inside the skin

P is the power per unit length (i.e., equal to the total power applied to the skin surface per width of the light beam in the direction perpendicular to the direction of scanning. P is in units of W/cm.

$\tau(d) = d^2/g\alpha$ is a period of thermal relaxation, where d is a diameter of the bulb, g is as previously indicated equal to 24 for a hair bulb, and α is the thermal diffusion coefficient of the tissue around the bulb.

For the destruction of a hair bulb, λ is in a range of 600 - 1200 nm and is preferably in a range of 670 - 1100 nm. In this range, $k(\lambda)$ varies from 1 - 0.1 and decreases with increasing wavelength. $\psi(z, \lambda)$ in this range increases with wavelength because of the weakening of the skin scattering properties and decreases with depth. At a depth of 3-5 mm where a hair bulb in its anagen stage is typically located, this value, which is sometimes referred to as radiance attenuation, is in the range of 0.1 - 0.5. This value may be significantly increased where focusing techniques to be described later are used. With focusing, the reflection coefficient of light from the skin can be 20% - 70%. Further, reflection of light scattered from the skin back into it by various means to be described increases the radiance in the zone of the hair bulge or in a hair bulb 1.2 - 2.5 times. Thus, the devices of this invention can allow $\psi(z, \lambda)$ to be increased to 0.5 - 1.

From the above, it can be seen that, once the geometry of the systems has been selected, the temperature at the bulb is directly proportional to the applied power P and is inversely proportional to the velocity V in a more complex way. Fig. 15 illustrates the dependence of maximum temperature at a hair bulb on scanning velocity V for typical parameters. The curve of Fig. 15 is calculated assuming $a = 0.3$ cm, $k = 0.5$, $\psi = 0.5$, $P = 40$ W/cm², $d = 0.03$ cm. From Fig. 15, it is seen that at low scanning velocities, T_m does not depend on scanning velocity and is equal to

$$T_m = \frac{6 \cdot P \cdot d \cdot k \cdot \psi}{g \cdot \alpha \cdot c \cdot \rho \cdot a} + T_0 \quad (8)$$

When the scanning velocity exceeds

$$V_m = \frac{g \cdot a \cdot \alpha}{3 \cdot d^2} \quad (9)$$

temperature T_m starts to decrease.

When V is less than V_m , the average temperature of the hair bulb does not change with changing velocity, but selectivity of thermal damage decreases. Thus, by decreasing the velocity of scanning, it is possible to increase the diameter of the zone of thermal damage around the hair bulb. Maximum scanning velocity depends on the hair bulb dimension and decreases as the size of the follicle increases. Fig. 16 shows the dependence of T_m for a hair bulb on the power per unit length P . For a treatment period of less than 1 second, denaturation of protein structures is observed at temperature exceeding 65°C. From Fig. 16, it is seen that maximum

temperature T_m at a hair bulb is also a function of the power P per unit length. For a treatment of less than 1 second, denaturization of protein structures is observed to occur at temperatures exceeding 65°C. Fig. 16 also illustrates that the power required to cause thermal damage in a hair bulb is inversely proportional to the size of the hair bulb (i.e., thermal damage is caused at a lower power for a large bulb than for a small bulb).

Thus, for hair removal, and regardless of the embodiment utilized, the following parameters would apply:

1. Wavelength: 600 - 1200 nm;
2. average power per length unit: 5 - 150 W/cm;
3. width of beam along direction of scanning: 0.05 - 5 mm;
4. scanning velocity: 0.01 - 10 cm/s;
5. temperature of cooling: -20°C - +30°C.

For preferred embodiments, optically transparent section 50 is also cooled by thermal element(s) 56b so as to prevent, or at least limit, heating of epidermis 12 in the treatment area during irradiation. This cooling effect is also a function of the scanning velocity and is particularly critical where irradiation used is of a wavelength which preferentially targets melanin, as is for example the case for certain hair removal treatments. Since there is a high concentration of melanin at DE junction 16, it is desirable that V be slow enough so as to permit heat produced at the DE junction to be removed through the cooled waveguide or other cooled optically transparent element 50. The maximum scanning velocity at which the cooling effect becomes noticeable for a given depth z is given by,

$$V_{\max} = \frac{4 \cdot L_2 \cdot \alpha}{z^2} \quad (10)$$

Where epidermis 12 to be cooled has a thickness of approximately 100 μm and the length L_2 is approximately 1 mm, $V_{\max} = 6 \text{ cm/s}$.

Further, as indicated earlier, the pressure applied to the skin by head 24 in general, and by the skin-contacting surface of element 50 in particular, has a number of advantages, including improving the optical transmission (i.e., reducing scattering) for radiation passing through the skin. The head moving in the direction 28 over area 10 of the skin also stretches the skin in the direction of scanning resulting in an additional increase in skin transmission and thus the depth

of electromagnetic wave penetration into the skin. Further, when the target is for example a hair follicle, the stretching of the skin turns the follicle to cause the radiation to impinge on a larger portion of the follicle and brings the follicle nearer to the skin surface.

Section 54 continues to cool the epidermis after irradiation to further guard against potential thermal damage to the skin. Unlike lengths L_1 , L_2 and L_4 which are fairly critical, the length L_3 is not critical. The purpose of this section is to assure that the epidermis is not overheated and, if the prior sections are effective in keeping the epidermis temperature down, section 54 may not be required.

Since it is generally desirable to decrease the time element 50 is over the target, it is generally desirable that L_2 be kept small. However, in order to achieve more rapid treatment, a significant beam aperture is desirable. This suggests that the dimension of the beam perpendicular to the direction of movement should be relatively large, resulting in an aperture for the skin contacting surface of element 50 which has an astigmatic shape, which shape may also be asymmetric. Fig. 6 illustrates two such shapes, namely an oval 66 (Fig. 6a), and a series of adjacent light pipes 76a, 76b as shown in Fig. 6b, the light pipes of Fig. 6b being discussed in greater detail in conjunction with Fig. 4. These shapes are just examples of astigmatic shapes for an optical aperture, and many other astigmatic shapes are within the contemplation of the invention.

Further, in order to deliver the radiation to a significant depth (i.e., greater than 1 mm) efficiently, large diameter beams are generally required to overcome the effect of scattering. With astigmatic beams of the type shown in Fig 6, it is therefore desirable that focusing of the beam in a direction perpendicular to the direction of scanning be used. One way of achieving this is through use of a cylindrical lens 70 such as is shown in Fig. 9 which lens has a small radius of curvature (for example less than 10 mm). However, such focusing can perhaps be better achieved through use of a head 24C such as that shown in Fig. 4. This head has a section 52 which functions in the same way as section 52 of head 24A to pre-cool or pre-heat the area under treatment. Section 52 is separated from a section 72 of the head by a layer of thermal insulation material 74. Section 72 is also formed of a metal or other material having good thermal conduction properties. Two rows of micro-optic elements 76a and 76b are provided which extend through section 72 and are angled so that their focuses are combined along a common line located at the target depth. Microlenses may be included at the distal ends of elements 76 to enhance focusing. This technique allows the beams to be targeted into the skin at angles greater

and can be achieved using optical systems and more effectively compensates for the scattering of radiation in the skin. Section 72 would be cooled, preferably by a number of thermoelectrical elements 56b, so as to provide both pre-cooling of the epidermis prior to irradiation, cooling of the epidermis during irradiation, and post-cooling of the epidermis. Section 72 can thus perform the cooling functions of sections 50, 52 and 54 of for example the embodiment of Fig. 2. Thus, for this embodiment of the invention, section 52 can be used as a pre-heater or can be eliminated.

Fig. 4 also illustrates some additional features. First, it shows an optical channel 78 which can be connected to a suitable detector in controls 34 for detecting the scan velocity of head 28. Other techniques which will be discussed in conjunction with Fig. 10 may also be used for performing this function. Detecting scan velocity permits controls 35 to operate output 40 if the scan velocity is detected to be outside of desired ranges so as to alert the operator so that the rate may be increased or decreased as appropriate. For example, the output may be a red or a green light on some portion of applicator 22 or a console associated therewith, might be a voice, or buzzer or other audio alert to the operator, might be a vibrator in the handle 26, or might be some other appropriate warning to the operator. In the event the rate is detected as being so slow (or even no movement at all) as to present a potential danger of injury to the patient, controls 34 might also deactivate source 30 so as to protect the patient.

One problem with radiation treatments is that a significant percentage of the radiation applied to the skin is reflected back or backscattered by the skin and lost. Various schemes have been proposed in the past for retroreflecting such radiation back into the skin, including for example putting some type of reflector in section 50. Sections 52 and 54 might also have a reflective coating on their skin contacting surfaces to reflect such radiation back into the skin. Section 72 is particularly useful for this purpose since the entire skin-contacting surface 80 of this section may be formed of highly reflective material, or have a highly reflective coating formed thereon. By redirecting most of the radiation back into the skin, the intensity of radiation inside the skin can be increased 1.2 to 2.5 times.

Fig. 5 shows a head 24D an embodiment of the invention which differs from that shown in Fig. 4 only in that there is a recessed channel 84 formed in skin-contacting surface 80 of section 72, and that optical channels 76a and 76b terminate on opposite sides of channel 84, with their focal point being at a point in the recess, for example at the substantial center thereof. A hose 86 is connected at one end to the top of channel 84 and at the other end to a source of negative pressure. As head 24D moves in direction 28 across the patient's skin, folds of the

patient's skin are drawn into channel 84. The size of channel 84 is selected such that the target is included in the fold of skin drawn into channel 84 and is irradiated from both sides by radiation applied to optical channels 76. For example, if head 24D is being used for hair removal, channel 84 might be 1 to 6 millimeters wide and 1 to 6 millimeters deep, a size which would generally result in the fold having only a single hair follicle in the plane shown in the figure, although multiple hair follicles may be in the channel along its long dimension. The configuration of Fig. 5 has several advantages. First, it reduces the distance for radiation to reach the target and more effectively focuses radiation on the target. Second, if the channel is formed of an optically reflective material, the walls of channel 84 reflect substantially all of the radiation leaving the skin back into the fold, providing for very efficient irradiation.

While in Fig. 5 it is assumed that a line connected to a vacuum or other source of negative pressure is utilized to draw a fold of skin into channel 84, a bellows or other suitable mechanism could also be utilized for drawing the skin into channel 84 or, as shown in Fig. 7, a head 24E could be provided having a channel 84' formed in a body 72' of a thermal conductive material, which channel is shaped so that a fold of skin 90 which includes the target 92 is forced into channel 84' as head 24E is moved in direction 28 over the patient's skin. Successive folds of the patient's skin would be pushed into channel 84' as the head moves so as to provide substantially uniform irradiation of the skin in treatment area 10. Except that a pre-heater section 52 is not included, the embodiment of Fig. 7 would otherwise operate in substantially the same way as in the embodiment of Fig. 5 and would afford substantially the same advantages.

Fig. 8 shows a head 24F which differs from those previously described in that it has four sets of optical channels 76, channel 76a, 76b, 76c, and 76d, which for this embodiment are merely light paths through a transparent block or air, each of which is fed by a corresponding flexible waveguides 32a-32d, respectively. All of the optical channels 76 are angled so as to be substantially focused at target depth 92. Body 72'' is curved to facilitate the placement of channels 76 and also has a reflecting top surface 93. In addition to components previously mentioned, Fig. 8 also includes a line 94 leading from a thermocouple or other suitable temperature sensor mounted close to surface 80 or in surface 80. Temperature sensor line 94 connects to controls 34 and may be utilized to control epidermal temperatures or for other suitable purposes.

Fig. 9 shows still another embodiment of the invention which, as previously indicated, utilizes a cylindrical lens 70 having a transparent window 96 against which is mounted a

radiation source 98, which may for example be a laser diode bar, a lamp with a reflector, or other radiation source which is small enough to be mounted in the handpiece. A reflection plate 100 is provided to perform the retroreflection function for back scattering light. Fig. 9 also shows a kinematic motion sensor 102 which may either supplement optical motion sensor 73 or may be
5 used in lieu thereof. Kinematic motion sensor 102 may for example be a wheel which turns as cylindrical lens 70 is moved over the skin surface to provide a signal to controls 34 indicative of scan velocity. Temperature control element 56 is shown as being in contact with both lens 70 and reflection plate 100 so as to cool both elements, thereby providing both pre-cooling of the treatment area and cooling during irradiation. There is preferably a second element 56 on the
10 opposite side of cylinder 70 in contact with plate 100 on the trailing side of the lens which is operative both to further cool the lens and to cool reflection plate 100 and the portion thereof trailing the lens to provide post-cooling. As indicated previously, cylindrical lens 70, particularly if it has a relatively small diameter, for example of less than 20 mm, is also operative to focus the radiation at target 92 and partly compensate the scattering effect of skin. Except as
15 indicated above, the embodiment of Fig. 9 operates substantially the same as the prior embodiments to provide scanned CW dermatologic treatment. It should also be noted that, while Fig. 9 is the only embodiment showing the radiation source 98 located in head 24 as opposed to the radiation being applied to the head from an external source 30 through optical leads 32, an external source 30 or an internal source 98 for the head is interchangeable for all embodiments, so that any of the prior embodiments may have an internal radiation source 98 in lieu of the
20 arrangement shown, and the embodiment of Fig. 9 may have an external radiation source with optical leads 32 impinging on transparent window 96. For an embodiment such as that shown in Fig. 8, a separate laser diode bar or bars 98 might for example be provided for each of the optical channels 76a-76d.

25 Figs. 10A and 10B show still another handpiece 24H suitable for practicing the teachings of the invention. This handpiece differs from those previously shown in that rather than radiant energy being applied directly to the optical waveguide, lens or other transparent component through which radiant energy is applied to the patient's skin, optical lines 32 terminate in a cavity 106 formed in a body 108 of copper or of some other material having good thermal conduction
30 properties. The walls of chamber 106 are polished, coated or otherwise treated to have highly reflective, and preferably totally reflective, surfaces. The advantage of the configuration shown in Fig. 10 with chamber 106 is that radiant energy enters cylindrical lens or astigmatic

microobjective 70' at a variety of angles which can be focused by the lens/microobjective to the desired depth in the skin, the focusing action being more efficient when the light enters the lens at a variety of angles than at a single angle. Cylindrical lens 70' may be mounted in body 108 either rigidly, as for the embodiment of Fig. 9, or may be mounted for rotation in the body.

5 Rotation of the lens facilitates movement of the head over the patient's skin, but prevents the desired stretching of the skin. However, a rotating lens is within the contemplation of the invention. Thermal elements 56 cool body 102, resulting in both pre-heating, cooling and post-cooling of the epidermis and also resulting in the cooling of cylindrical lens 70' which cools the epidermis during irradiation. Body 108 has reflective skin-contacting surfaces 80 to retroreflect

10 back scattering light from the patient's skin. Fig. 10 also illustrates kinematic motion sensor 102 and a thermocouple or other suitable temperature sensor 94. Except for the differences discussed above, the embodiment of Fig. 10 functions substantially the same as the embodiments previously discussed.

Figs. 11a-11c illustrate still another embodiment 24I for the head. With this embodiment,

15 cylindrical lens 112, which for example is formed of sapphire, is treated to normally have total internal reflection so that light or other radiation entering the lens through optical line 32 is reflected through the lens and exits through optical lines 32'. However, when lens 112 is in contact with the patient's skin as shown in Fig. 11c, the total internal reflection at the skin-contacting surface is broken due to the change of index of refraction at this surface so that light

20 energy is emitted from the lens into the patient's skin. The use of the total internal reflection lens 112 of Fig. 11 is a safety feature which assures that radiation is not applied to a patient or other person unless handpiece 24 is in contact with a patient's skin in the area to be treated. Except for this difference, the embodiment of Fig. 11 functions in the manner described for previous embodiments and components such as a housing for pre- and post-cooling, a chiller for the lens,

25 motion sensors, etc. of prior embodiments might also be used with this embodiment.

While for the embodiments of the invention described so far radiation energy is applied in parallel along the length of the head during irradiation, Figs. 12a and 12b illustrate embodiments of the invention where light is rapidly scanned. In Fig. 12a, radiant energy applied to the head over a line 32 impinges on a deflector 120 which is oscillated at a rate such that the

30 impinging radiation is scanned in the direction indicated by arrows 122 at the rate previously indicated across a cylindrical lens 70''. In Fig. 12b, the impinging radiation 32 is also applied to an oscillating deflector 120 which scans the beam into optical fibers 124. Each optical fiber

terminates in a microlens 126 mounted in a plate 128 of a highly thermal conductive material. Plate 128 also preferably has a highly reflective skin-contacting surface 80. So long as the scan rate of deflector 120 is high enough, the radiation outputted from cylindrical lens 70'' or microlenses 126 is CW radiation as this term has been previously defined, and this system
5 operates substantially the same as for previous embodiments. Again, for purposes of simplifying the drawings, elements such as thermal elements 56, motion sensor 78 and 102, and temperature sensors 94, are not shown in Figs. 12a and 12b.

Fig. 13 is included to illustrate that pre-heating of the treatment area, while more easily facilitated with the CW embodiments heretofore described, is not limited to such embodiments
10 and may be utilized with a standard pulsed head of a type used in some prior art systems. In Fig. 13, radiation, which may be pulsed radiation from a source 30, is applied through optical lead 32 to an optical waveguide 50 having thermal elements 56 in contact therewith. Waveguide 50, having a focusing skin-contacting end 132, is mounted in a suitable housing, a portion 130 of which is shown in the figure. Thermal elements 56, which are thermoelectric elements, for the
15 embodiment shown, but may be other type of cooling, may be operated to heat waveguide 50 for a time interval sufficient to heat the skin to the depth z of the target. Either the same or a different set of thermoelectric elements 56 may then be operated to cool waveguide 56 for a duration sufficient to cool epidermis 12 to the DE junction 16, at which time source 30 is energized to apply radiation through waveguide 50 to the target. Cooling of waveguide 50
20 continues during this period to maintain the epidermis at a desired temperature during irradiation and the cooling of waveguide 50 may be contained for some period of time after irradiation terminates to further protect the patient's skin. Further, while preheating has been shown and described above followed by epidermal cooling, and for many applications this is clearly preferable, it is also within the contemplation of the invention to do preheating without
25 subsequent cooling. Head designs such as those shown in Figs. 2, 4, and 5 (either with or without portion 52, and generally without), 8-12, might also be used when operating in a pulsed mode. Operation with these heads in a pulsed mode could be similar to operation in a CW mode except that movement of the head would be stepped rather than continuous.

While a number of embodiments and variations thereon have been described above, it is
30 apparent that these embodiments are for purposes of illustration only and that numerous other variations are possible while practicing the teachings of this invention. For example, while in the discussion above it has been assumed that head 24 is manually moved over the treatment area,

this is not a limitation on the invention and various types of mechanical scanners could also be utilized, either alone or in conjunction with manual control. Further, while optical and kinematic movement measuring mechanisms have been shown, suitable thermal, electronic and magnetic movement measure mechanisms could also be used. Controls 34 would function to maintain the
5 required scan velocity for such scanner. Thus, while the invention has been particularly shown and described above with reference to preferred embodiments, the foregoing and other changes in form and detail may be made therein by one skilled in the art without departing from the spirit and scope of the invention which is to be defined only by the appended claims.

CLAIMS

1. Apparatus for effecting a selected dermatologic treatment on an area of a patient's skin including:
 - a source of continuous wave (CW) radiation at a wavelength appropriate for the selected
 - 5 dermatologic treatment; and
 - a head having at least one optically transparent channel formed therethrough, each said channel having a proximal end connected to receive CW radiation from said source and a distal end terminating in a surface which is smaller than the said area of the patient's skin and which is formed to be in contact with the patient's skin as the head is moved at a selected rate over said
 - 10 area.
2. Apparatus as claimed in claim 1 wherein the head has a portion which moves over each successive segment of said area before said at least one optical channel, which portion is of a thermally conductive material; and including a thermal component which controls the
- 15 temperature of said portion, and thus of the skin area prior to treatment.
3. Apparatus as claimed in claim 2 wherein said component cools said portion of the head, and thus cools the skin area prior to treatment.
- 20 4. Apparatus as claimed in claim 2 wherein said component heats the portion of the head, and thus heats the skin area prior to treatment.
5. Apparatus as claimed in claim 2 wherein said portion of the head is divided into a first portion and a second portion which are thermally insulated from each other, said first portion
- 25 being ahead of said second portion, and wherein said component has a first component which heats said first portion and a second component which cools said second portion.
6. Apparatus as claimed in claim 1 wherein said head includes a portion which moves over each successive segment of said area after said optically transparent channel, which portion is of
- 30 a thermally conductive material, and including a component for cooling said portion.

7. Apparatus as claimed in claim 1 including a handle projecting from said head suitable for use by an operator to move the head over the area, and an indicator of the rate of head movement.
8. Apparatus as claimed in claim 1 wherein said at least one optically transparent channel
5 includes a single elongated channel having an optical channel extending at least part-way through the channel and projecting from the bottom of the head.
9. Apparatus as claimed in claim 8 including a component for cooling said optical channel, the cooled optical channel removing heat from the skin in said area under treatment as said
10 optical channel, in thermal contact with the skin, passes thereover.
10. Apparatus as claimed in claim 1 wherein said head is formed to enable an operator of the apparatus to apply at least sufficient pressure to the head as it contacts the skin to assure at least
15 on of good thermal and optical contact between skin-contacting surfaces of the head and the patient's skin in said area.
11. Apparatus as claimed in claim 1 wherein said at least one optically transparent channel includes a plurality of first optical channels angled at a first angle and a plurality of second optical channels angled at a second angle, said first and second angles being selected so that light
20 passing through the first and second optical channels converge at a selected depth.
12. Apparatus as claimed in claim 11 wherein said selected depth is at a depth in the area under treatment at which the dermatological treatment is to occur.
- 25 13. Apparatus as claimed in claim 11 including a recess formed in a surface of the head in contact with the patient's skin, said recess being at the distal end of said optical channels, said selected depth being at a selected location in said recess, and including means for moving skin in said area under treatment into said recess as the recess passes thereover.
- 30 14. Apparatus as claimed in claim 13 wherein said means for moving skin into said recess includes a source of negative pressure connected to said source.

15. Apparatus as claimed in claim 13 wherein said means for moving skin into said recess includes said recess being shaped to force successive folds of skin therein as the head is moved over said area with said surface of the head in pressure contact with the patient's skin.
- 5 16. Apparatus as claimed in claim 13 wherein the apparatus is a hair removal apparatus, and wherein said recess is elongated in a direction perpendicular to the direction in which said head is moved and is sized so as to normally receive therein a fold of the patient's skin which contains several hair follicles extending in the elongated direction.
- 10 17. Apparatus as claimed in claim 11 wherein said head has a portion in contact with the patient's skin in segments thereof receiving radiation, and including a thermal component which cools said portion of the head.
- 15 18. Apparatus as claimed in claim 1 wherein said transparent channel includes a cylindrical lens.
19. Apparatus as claimed in claim 18 wherein said cylindrical lens is mounted to rotate as said head is moved over said area.
- 20 20. Apparatus as claimed in claim 18 wherein said lens is treated so as to normally have total internal reflection, said total internal reflection being broken at a surface of the lens in contact with a patient's skin.
- 25 21. Apparatus as claimed in claim 1 including a mechanism for measuring the rate at which said head is being moved over said area.
22. Apparatus as claimed in claim 21 including controls responsive to said mechanism for determining if the head is moving over said area at a rate within a predetermined range and for providing a selected output in response to a determination that the head is moving at a rate
30 outside of said range.

23. Apparatus as claimed in claim 21 including controls responsive to said mechanism for determining if the head is moving at a rate which poses a danger of injury to the patient and for terminating the application of radiation through said at least one channel to the patient's skin in response to a danger-of-injury indication.

5

24. Apparatus as claimed in claim 1 wherein the distal end of said at least one transparent channel has an astigmatic shape, being narrower in the direction of head movement than in a direction normal thereto.

10 25. Apparatus as claimed in claim 24 including a mechanism for scanning said CW radiation across said at least one transparent channel.

26. Apparatus for effecting a selected dermatologic treatment on a selected volume of a patient's skin located at a depth d which is below the DE junction comprising:

15 a first mechanism for preheating the patient's skin to raise the selected volume to a selected temperature while not heating any portion of the skin to a temperature sufficient to cause thermal damage thereto;

a second mechanism for cooling the patient's epidermis above said selected volume to a temperature below normal body temperature without resulting in any appreciable cooling of
20 said selected volume; and

a third mechanism for applying electromagnetic radiation to said selected volume through said cooled epidermis, the radiation being of a wavelength, energy and duration sufficient, in conjunction with the preheating, to effect thermal damage to at least a selected biological component within said selected volume without causing thermal damage to the cooled epidermis.

25

27. Apparatus as claimed in claim 26 including at least one thermal element operable in a heating or cooling mode, said at least one thermal element forming part of said first mechanism and said second mechanism.

30 28. Apparatus as claimed in claim 27 wherein said at least one thermal element is at least one thermoelectric element.

29. Apparatus as claimed in claim 26 wherein said first mechanism includes a source of electromagnetic radiation at a selected wavelength and energy sufficient to cause heating of at least selected biological substances in said selected volume, but not sufficient to cause thermal damage to the patient's skin.

5

30. Apparatus as claimed in claim 29 wherein said source of electromagnetic radiation is operable at controllable energy levels and is part of both said first and said third mechanisms at selected energy levels for each.

10 31. Apparatus as claimed in claim 26 wherein said second mechanism is operative both before and during operation of the third mechanism to protect the epidermis from thermal damage.

32. A method for effecting a selected dermatologic treatment on an area of a patient's skin including the steps of:

15 placing a head having at least one optically transparent channel formed therethrough in contact with the patient's skin in said area, said at least one channel having a distal end in contact with a segment of the patient's skin which segment is smaller than said area,

moving said head, while in contact with the patient's skin, at a selected rate over said area, and

20 applying CW radiation of a wavelength appropriate for the selected dermatologic treatment through the at least one channel to the patient's skin.

33. A method as claimed in claim 32 including the step of utilizing the head to control the temperature of segments of the patient's skin in the area prior to each said segment being moved
25 over by said at least one channel.

34. A method as claimed in claim 33 wherein said step of controlling temperature includes the step of heating each said segment to a temperature below that at which thermal damage occurs in the skin.

30

35. A method as claimed in claim 33 wherein said step of controlling temperature includes the step of cooling each said segment.

36. A method as claimed in claim 33 wherein said step of controlling temperature includes the steps of heating each said segment to a selected depth, and then performing epidermal cooling for the segment.
- 5 37. A method as claimed in claim 32 including the step of utilizing the head to cool each segment in said area after radiation has been applied thereto through said at least one channel.
38. A method as claimed in claim 32 including the step of utilizing the head to cool each segment of the patient's skin as radiation is being applied thereto during said applying step.
- 10 39. A method as claimed in claim 32 wherein said moving step includes the step of applying at least sufficient pressure to said head to assure at least one of good thermal and optical contact between skin-contacting surfaces of the head and the patient's skin in said area.
- 15 40. A method as claimed in claim 32 wherein the surface of said head in contact with the patient's skin has a recess formed therein, and including the step of moving successive folds of the patient's skin into said recess as the recess passes thereover.
41. A method as claimed in claim 32 wherein said moving step includes the step of rolling
20 said head over said area while maintaining contact therewith.
42. A method as claimed in claim 32 including the step of measuring the rate at which said head is being moved over said area.
- 25 43. A method as claimed in claim 32 including the steps of determining if the head is moving over said area at a rate within a predetermined range, and providing a selected output in response to a determination that the head is moving at a rate outside of said range.
44. A method as claimed in claim 32 including the steps of determining if the head is moving
30 at a rate which poses a danger of injury to the patient, and terminating the application of radiation through said at least one channel to the patient's skin in response to a danger-of-injury indication.

45. A method as claimed in claim 32 wherein the selected rate at which said head is moved over said area is fast enough so as to prevent significant thermal damage to the patient's skin, but slow enough so as to provide a sufficient dwell time over said area of the patient's skin to effect the selected dermatologic treatment.

5

46. A method as claimed in claim 32 wherein during said moving step, the head is moved substantially continuously at a substantially constant rate.

47. A method for effecting a selected dermatologic treatment on a selected volume of a patient's skin located at a depth d which is below the DE junction including the steps of:

10 (a) preheating the patient's skin to raise the selected volume to a selected temperature while not heating any portion of the skin to a temperature sufficient to cause thermal damage thereto;

(b) cooling the patient's epidermis above said selected volume to a temperature below normal body temperature without resulting in any appreciable cooling of said selected volume; and

15 (c) applying electromagnetic radiation to said selected volume through said cooled epidermis, the radiation being of a wavelength, energy and duration sufficient, in conjunction with the preheating, to effect thermal damage to at least a selected biological component within said selected volume without causing thermal damage to the cooled epidermis.

20

48. A method a claimed in claim 47 wherein step (b) is performed both before and during step (c).

25 49. Apparatus for effecting a selected dermatologic treatment on a selected volume of a patient's skin located at a depth d which is below the DE junction including:

a first mechanism for preheating the patient's skin to raise the selected volume to a selected temperature while not heating any portion of the skin to a temperature sufficient to cause thermal damage thereto; and

30 a second mechanism for applying electromagnetic radiation to said selected volume, the radiation being of a wavelength, energy and duration sufficient, in conjunction with the

preheating, to effect thermal damage to at least a selected biological component within said selected volume without causing significant thermal damage to surrounding tissue.

50. A head for use in apparatus for effecting a selected dermatologic treatment on an area of a patient's skin including:

a block formed of a material having good thermal transfer properties, and a plurality of first optical waveguide elements and a plurality of second optical waveguide elements extending through said block, said first and second optical waveguide elements being angled at first and second angles respectively, which angles are selected so that light passing through the first and second optical waveguide elements converge at a selected depth, said optical waveguide elements having radiation applied thereto appropriate for the selected dermatologic treatment.

51. A head as claimed in claim 50 wherein said selected depth is at a depth in the area under treatment at which the dermatological treatment is to occur.

15

52. A head as claimed in claim 50 including a recess formed in a surface of the head in contact with the patient's skin, said recess being at the distal end of said optical waveguide elements, said selected depth being at a selected location in said recess, and including means for moving skin in said area under treatment into said recess passes thereover.

20

53. A head as claimed in claim 52 wherein said means for moving skin into said recess includes a source of negative pressure connected to said source.

54. A head as claimed in claim 50 wherein said block has a skin contacting surface which retroreflects radiation leaving the patient's skin.

25

55. A head as claimed in claim 50 including a mechanism for controlling the temperature of said block.

56. A method for effecting a selected dermatologic treatment on a selected volume of a patient's skin located at a depth d which is below the DE junction including the steps of:

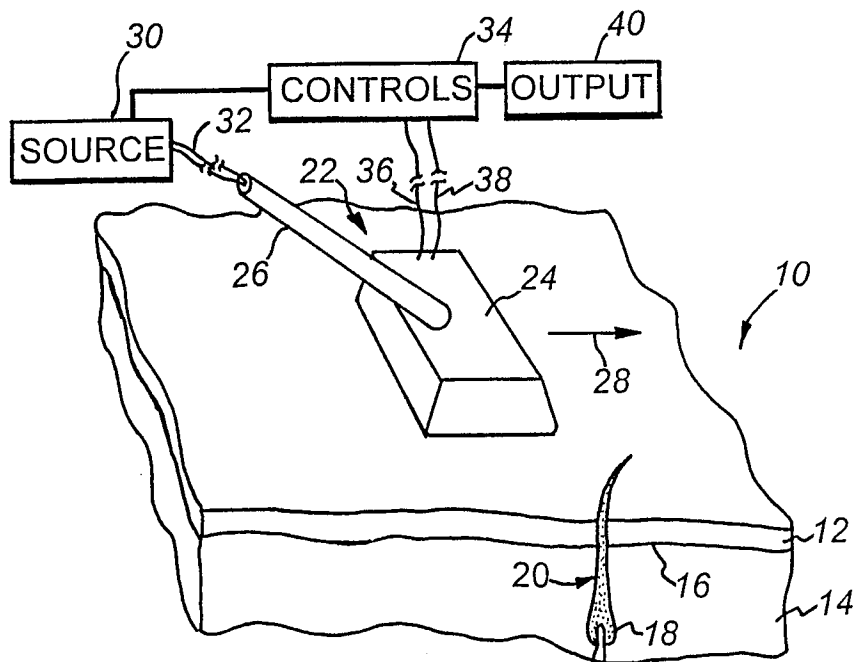
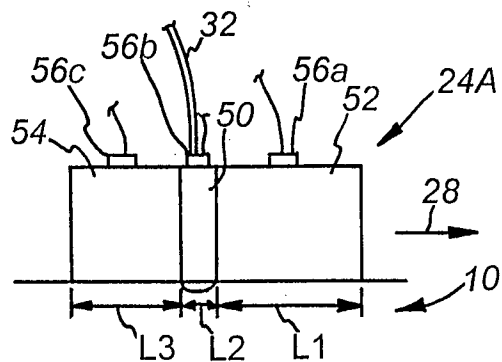
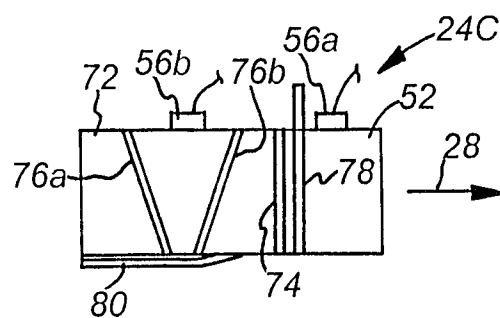
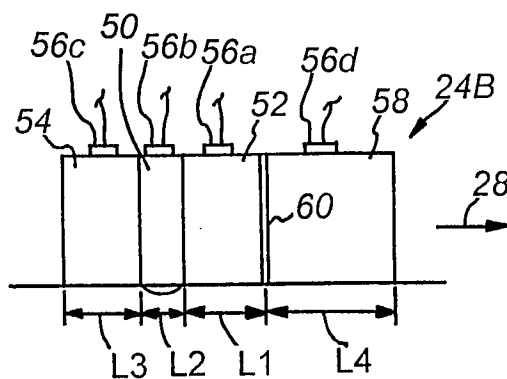
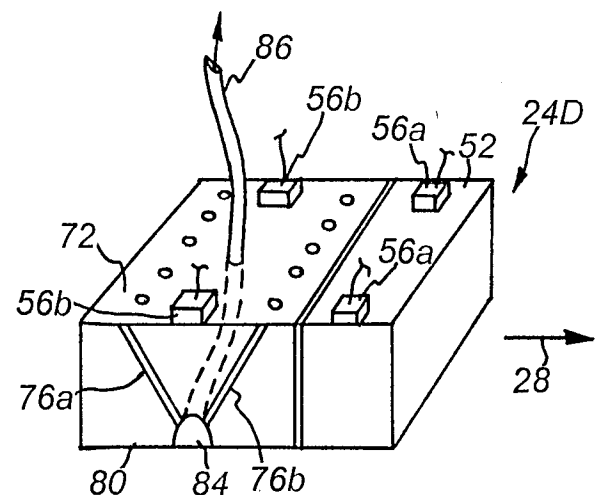
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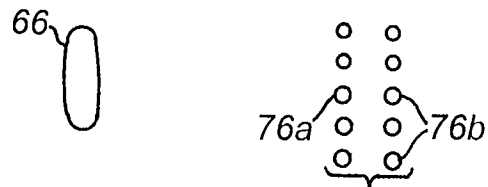
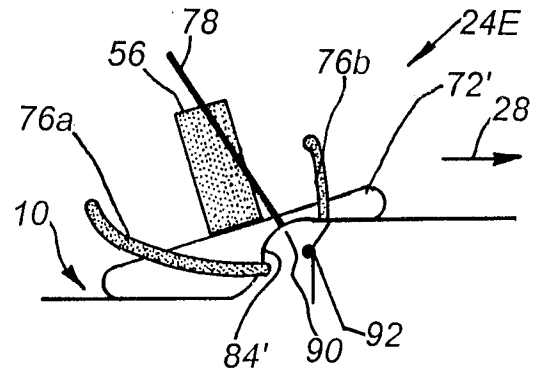
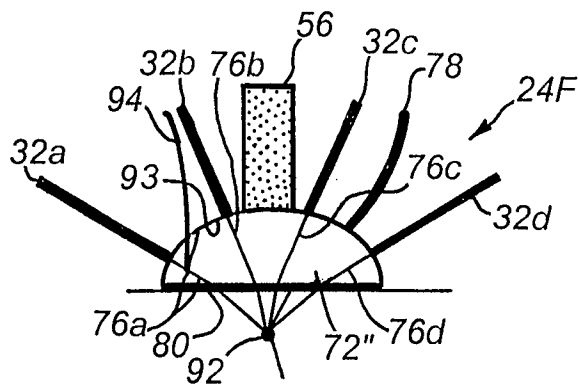
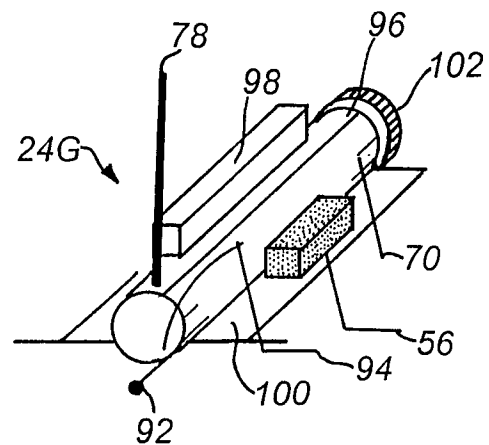
(a) preheating the patient's skin to raise the selected volume to a selected temperature while not heating any portion of the skin to a temperature sufficient to cause thermal damage thereto;

(b) applying electromagnetic radiation to said selected volume, the radiation being of a
5 wavelength, energy and duration sufficient, in conjunction with the preheating, to effect thermal damage to at least a selected biological component within said selected volume.

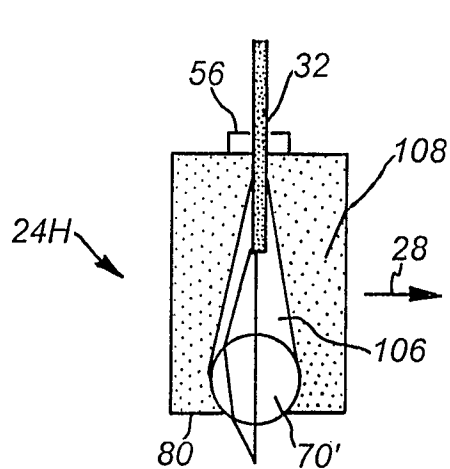
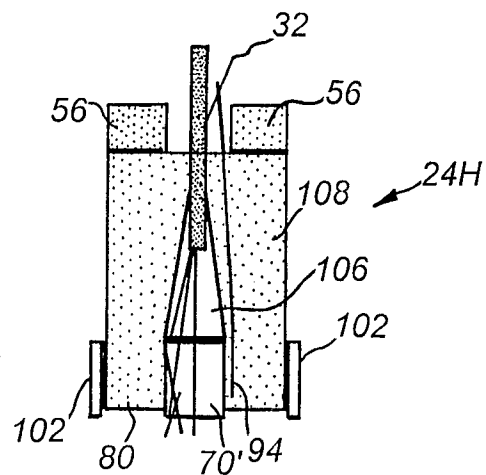
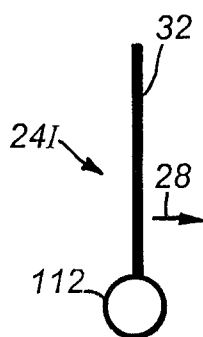
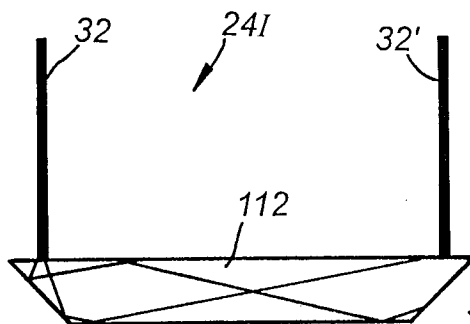
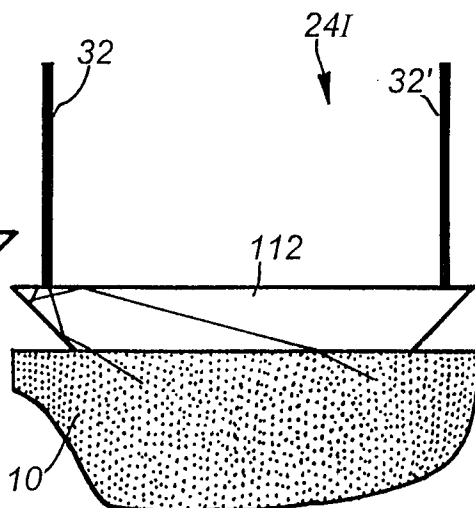
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**Fig. 1****Fig. 2****Fig. 4****Fig. 3****Fig. 5**

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**Fig. 6A Fig. 6B****Fig. 6****Fig. 7****Fig. 8****Fig. 9**

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**Fig. 10A****Fig. 10B****Fig. 10****Fig. 11A****Fig. 11B****Fig. 11C****Fig. 11**

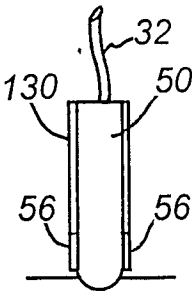
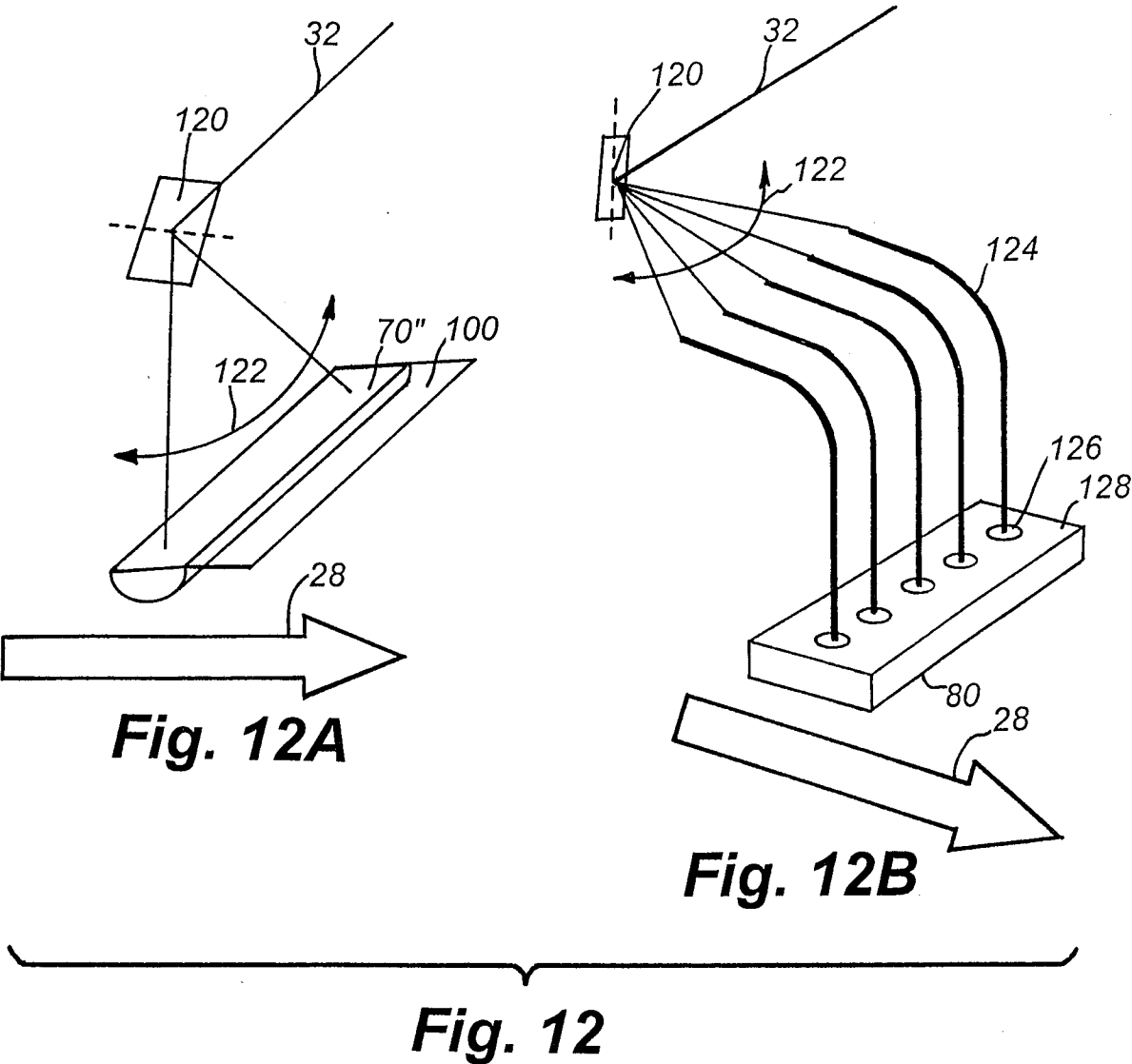
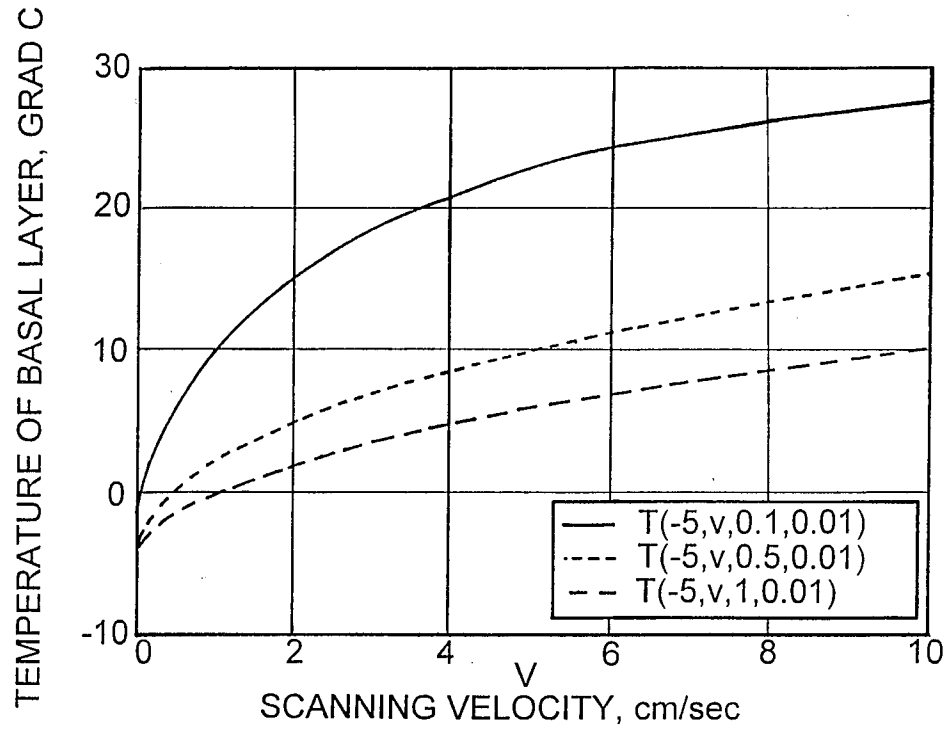
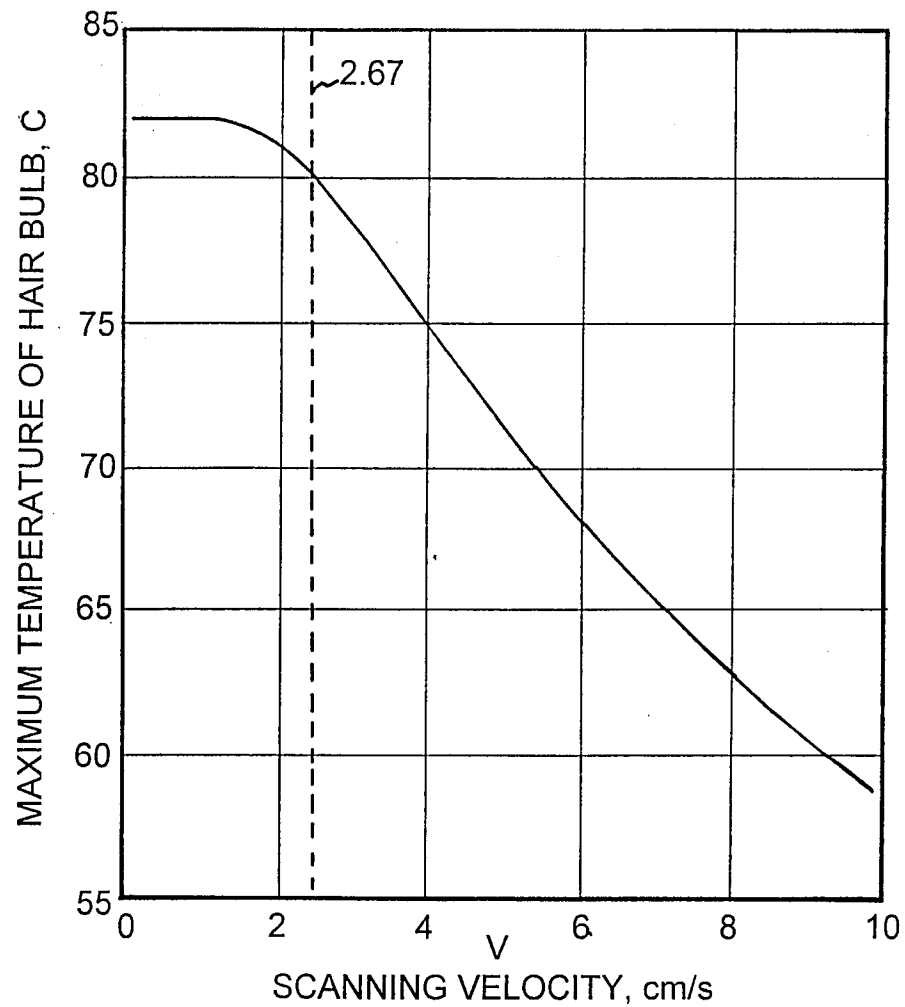
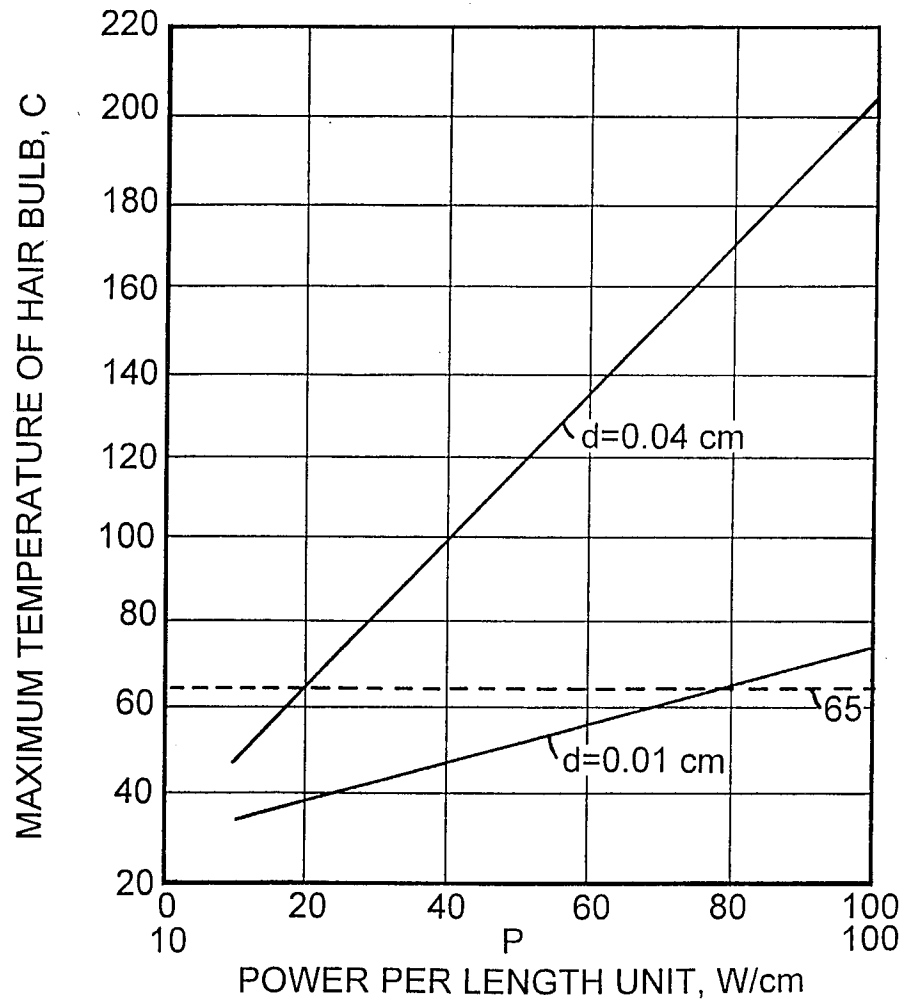


Fig. 13

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**Fig. 14****Fig. 15**

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**Fig. 16**

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/09600

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61F 2/00

US CL :607/100

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 606/2, 9, 36; 607/88-90, 93, 96, 100-102

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C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 5,057,104 A (CHESS) 15 October 1991, entire document.	26, 27, 29-31, 47-49 ----- 5, 6, 28, 56
X,P ----- Y,P	US 5,683,380 A (ECKHOUSE et al) 04 November 1997, entire document.	1-4, 8, 10, 12, 13, 15, 16, 18, 24, 25, 32, 39-41, 45, 46 ----- 11, 14, 19, 20, 50-55

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

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INTERNATIONAL SEARCH REPORT

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y,P	US 5,662,644 A (SWOR) 02 September 1997, entire document.	7, 9, 17, 21-23, 33-38, 42-44

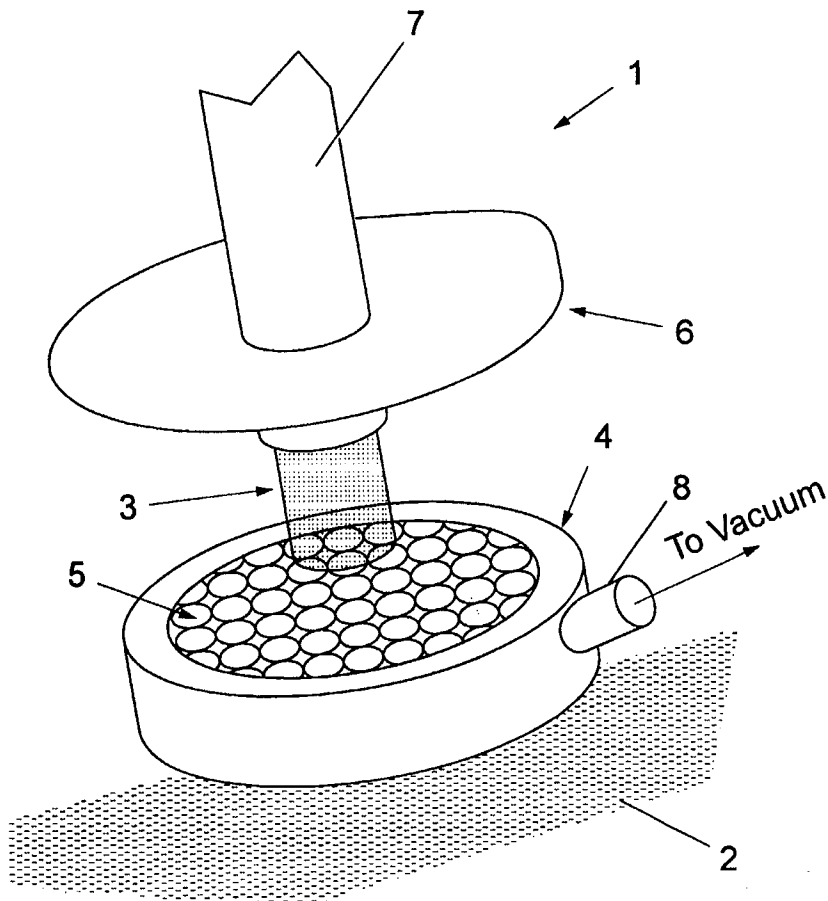
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(21) International Application Number: PCT/GB98/01523 (22) International Filing Date: 26 May 1998 (26.05.98) (30) Priority Data: 9710562.1 23 May 1997 (23.05.97) GB (71) Applicant (for all designated States except US): MEDICAL LASER TECHNOLOGIES LIMITED [GB/GB]; Unit 4, Belleknowes Industrial Estate, Inverkeithing, Fife KY11 1HY (GB). (72) Inventor; and (75) Inventor/Applicant (for US only): COLLES, Michael, John [GB/GB]; Boglesknowe, Hartree by Biggar, Lanarkshire ML12 6JJ (GB). (74) Agent: MURGITROYD & COMPANY; 373 Scotland Street, Glasgow G5 8QA (GB).		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i>

(54) Title: APPARATUS AND METHOD FOR DELIVERY OF LIGHT TO SKIN

(57) Abstract

Improvements to a system for the process of hair removal which employs a collimated laser beam delivered to a target. These improvements include a reflector for reflecting back light scattered from the surface and improving light coupling into the tissue, use of an array of micro lenses for focusing the incident beam, and an annular ring to thin the epidermis and upper dermis to reduce blood volume in the illuminated area, and increase flux density at significant depths.



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1
2 Apparatus and method for delivery of light to skin

3
4 This invention relates to light delivery and in
5 particular to a apparatus and method for delivery of a
6 beam of light to a target area beneath the surface of
7 the skin.

8
9 Most particularly this invention relates to an
10 apparatus and method designed to improve the delivery
11 of laser or other light to targets underneath the skin
12 surface especially, but not solely, to assist in
13 optical hair removal. That is, this invention relates
14 to the use of optical based techniques in dermatology
15 for the removal of unwanted stains, pigment, marks,
16 hairs, or other sub-surface features.

17
18 Lasers and, in some cases, other light sources have
19 found increasing use in dermatology for the treatment
20 or removal of sub-surface lesions. These techniques
21 have largely been based on the concepts of selective
22 photothermolysis. This implies that the laser
23 wavelength is chosen to match a characteristic
24 absorption associated with the target but not with the
25 surrounding tissue. Thus, absorption of the laser

1 light and the subsequent heating is largely restricted
2 to that target. In addition, the process also involves
3 choosing the duration of the laser pulse to maximise
4 the temperature of the target before significant
5 conduction to the surrounding tissue can take place.
6 For example, a 30 nanosecond pulse from a Nd:YAG laser
7 at $1.06\mu\text{m}$ is strongly and selectively absorbed in the
8 blue-black pigments of common tattoos. Since the
9 tattoo pigments accumulate in granules of micron size,
10 such a short pulse is almost wholly used to heat and
11 fragment the granule before significant heating of the
12 surroundings takes place.

13
14 More recently techniques have been described which
15 relate to the removal of unwanted hair using lasers.
16 In one approach a Nd:YAG laser similar to the one
17 mentioned above is used. Since there is little or no
18 natural selective absorption at this wavelength, an
19 external chromophore must first be applied and
20 persuaded to migrate down the hair shaft to the base to
21 provide an appropriate target.

22
23 In an alternative approach a ruby laser at 0.694nm is
24 used. In this approach the melanin content of the hair
25 shaft provides the selectively absorbing chromophore.

26
27 The ruby laser was introduced many years ago for
28 removal of tattoos. For tattoo removal the laser
29 output was "Q-Switched" - that is, the energy was
30 compressed to a pulse of only a few 10 's of
31 nanoseconds. Such a pulse, whilst ideal for tattoo
32 granule fragmentation, is neither necessary nor
33 desirable for the more thermal process of hair removal.

34
35 For hair removal, the ruby laser is operated in its so-
36 called "normal mode" wherein the pulse duration is

1 extended to about 1 millisecond. The real target is
2 not the hair itself. Following the selective
3 absorption of the laser light along the buried hair
4 shaft and the heating of the latter, the overall
5 process relies on the conduction of heat from the shaft
6 to surrounding tissue, in particular to two zones, the
7 first near the shaft base (papilla); and the second
8 approximately a third of the way down the shaft, known
9 as the bulge. Direct absorption into these zones is
10 possible, and can contribute to their heating since
11 they also contain an enhanced level of melanin. These
12 zones are believed to contain the cells responsible for
13 hair growth, and damage to them via this process of
14 laser heating should lead to permanent hair removal or
15 at least substantially delayed regrowth.

16
17 A simple approach is to apply light with the required
18 level of energy density to an area of skin. The level
19 is chosen to give sufficient heating to destroy the
20 target zones whilst leaving the surrounding tissue
21 undamaged. In practice this required level lies
22 between 10 and 50 J/cm².

23
24 Various techniques have been used or proposed to assist
25 in improving the efficiency of the process. These
26 techniques include precooling of the area, cooling
27 during the process, selective cooling of the epidermis
28 using millisecond cryogen spray, use of optical
29 transmitting gels to improve coupling into the tissue,
30 convex shaped applicators, and devices to draw folds of
31 skin which may receive radiation from either side.

32
33 Whereas there may be both advantages and disadvantages
34 to varying degrees in all of these approaches, it is
35 manifest that there is a need for a beam delivery
36 system that addresses the problems of sub-surface

1 targeting from both an optical and a biological
2 viewpoint.

3

4 According to a first aspect of the present invention
5 there is provided an apparatus for delivery of a beam
6 of light to a target area beneath the surface of the
7 skin comprising means to deliver a collimated light
8 beam, and light delivery means to increase the light
9 energy density at said target area while minimising the
10 light energy density at the surface of the skin.

11

12 Preferably said means to improve delivery comprises
13 means to improve effective light coupling into tissue.
14 Said means to improve effective light coupling may
15 comprise recovery means to recover light reflected on
16 incidence with the skin.

17

18 Said recovery means may comprise a reflective surface.

19

20 Preferably the apparatus comprises means to thin the
21 skin above the target area. Said means may stretch the
22 skin.

23

24 Preferably the apparatus comprises means to reduce
25 local blood flow in the target area.

26

27 Preferably the means to stretch the skin acts also to
28 reduce the local blood flow.

29

30 Preferably the apparatus comprises means to subject the
31 area adjacent the target area to vacuum suction.

32

33 Said means may comprise a member adapted to be sealed
34 to the skin and to subject the area of skin surrounding
35 the target area to a vacuum.

36

1 Preferably said member has an annular channel. Said
2 channel may be ring shaped or oval.

3 Preferably said channel is adapted to be positioned
4 with the channel opening in contact with the skin.

5

6 Preferably the apparatus comprises means to increase
7 light flux density at the depth of the target. Said
8 means may redistribute an incident collimated beam
9 prior to its incidence with the skin.

10

11 Said redistribution means may comprise an array of
12 lenses. Preferably said lenses are of short focal
13 length. Preferably said array is selected to increase
14 the flux density at a nominated depth.

15

16 Preferably the apparatus comprises recovery means to
17 recover light reflected on incidence with the skin;
18 means to thin the skin above the target; and means to
19 increase light flux at the depth of the target.

20

21 Preferably the light beam is a laser light beam.

22

23 The apparatus may further include known techniques such
24 as tissue precooling and/or selective cooling of the
25 epidermis and/or use of optical transmitting gels
26 and/or convex shaped applicators and/or devices to draw
27 folds of skin which may receive radiation from either
28 side and/or other features already known.

29

30 According to a second aspect of the present invention
31 there is provided a method for delivery of a beam of
32 light to a target area beneath the surface of the skin
33 comprising the step of using an apparatus according to
34 the first aspect of the invention.

35

36 According to a further aspect of the present invention

1 there is provided a method for delivery of a beam of
2 light to a target area beneath the surface of the skin
3 comprising the steps of directing a collimated light
4 beam onto the surface of the skin, and using a light
5 delivery means to increase the light energy density at
6 said target area while minimising the light energy
7 density at the surface of the skin.

8

9 Embodiments of the present invention will now be
10 described by way of example only with reference to the
11 accompanying drawings in which:

12

13 Figure 1 shows a apparatus in accordance with an
14 aspect of the present invention.

15

16 Figures 2a and 2b illustrate the effect on fluence
17 at the skin surface and at a given depth beneath
18 the surface, of increasing the area of surface
19 illumination of the skin;

20

21 Figures 2c and 2d also illustrate the effect on
22 fluence at the skin surface and at a given depth
23 beneath the surface, of increasing the area of
24 surface illumination;

25

26 Figure 2e is a graphical representation of the
27 rate of increase of the effective fluence at depth
28 with increase of surface beam diameter;

29

30 Figures 3a and 3b show a beam focusing
31 arrangements in accordance with an aspect of the
32 present invention;

33

34 Figure 4 illustrates means for recapturing
35 reflected light in accordance with an aspect of
36 the present invention; and

1 Figure 5 shows an annular ring in accordance with
2 an aspect of the present invention.

3
4 Referring to the drawings, this apparatus, generally
5 designated 1 is designed to provide a combination of
6 both optical and mechanical means of improvement of the
7 sub-surface flux density of a beam delivered by a beam
8 delivery system to the target areas. Although this
9 apparatus has its origins in improvements related to
10 beam delivery for hair removal, other optical processes
11 requiring selective sub-surface damage may benefit.

12
13 A beam delivery system normally comprises a light
14 source and means for its delivery to a target area. A
15 first improvement to this system is the provision of a
16 sealed annular ring 4 as shown in Figure 5. This
17 annular ring is placed adjacent the tissue surface 2
18 above the target. The region of surface skin in the
19 annulus is subject to a vacuum by connection of a
20 vacuum pump to vacuum outlet 8 and is thus drawn
21 upwards to form raised areas 11. In one dimension this
22 is similar to proposals for obtaining a fold of tissue
23 to allow transillumination. However the instant
24 configuration takes advantage of the fact that dermal
25 blood is taken towards the region 11 under vacuum in
26 the direction of arrows 10 and thus away from the
27 central circular core area 12.

28
29 Although the ruby laser wavelength corresponds to a
30 minimum in the absorption spectrum of blood, residual
31 absorption of blood remains a competing unwanted factor
32 in the utilisation of the laser light. Thus reduction
33 of local blood volume due to adjacent vacuum suction
34 provides an important advantage.

35
36 A second and more significant effect is that the

1 drawing up into the annulus of a small amount of tissue
2 13 effectively stretches the skin 2 throughout the
3 circular core 12. Even mild stretching of around 10%
4 of the diameter - 2mm in Figure 5 where the central
5 area has a diameter of 20mm - translates to a thinning
6 of the epidermis and upper dermis of 20%. Since the
7 reduction in light flux with depth into the skin is
8 exponential this thinning provides an increase in flux
9 density of as much as 80% at a depth of 3mm
10 corresponding to the depth of the papilla. This
11 effect, in conjunction with the reduction of the local
12 blood volume, reduces the required incident flux
13 density by a significant factor. These effects also
14 improve the selectivity of the process.

15

16 This aspect of the invention is thus directed
17 principally at providing a physical means of reducing
18 beneficially both the blood content of the tissue
19 immediately below the exposed area, and the thickness
20 through which light must penetrate to reach structures
21 at depths of several millimetres.

22

23 Both these effects, that is the biological and the
24 physical, combine to improve the fraction of light
25 fluence (energy per unit area) at the required depth
26 for a given fluence at the surface.

27

28 Usually if the target structures are at some
29 significant depth into tissue, a problem arises in
30 trying to balance the need for a minimum fluence at
31 depth required to effect the necessary damage, whilst
32 sparing structures nearer the surface that normally see
33 a significantly higher fluence. This aspect of the
34 invention acts directly to improve this situation and
35 thus helps in sparing surface tissue and components.

36

1 A handpiece incorporating such a ring 4 has its most
2 immediate application in a process such as hair removal
3 where selective damage to the follicles 2-4mm deep is
4 required. Other applications, for example the
5 visualisation of dermal blood vessel anatomy for
6 diagnostic purposes would also benefit.

7
8 The influence of light scattering in tissue is to
9 substantially increase the volume of tissue
10 experiencing some of the light compared with the
11 initially exposed area. The larger the initial area,
12 the less this affects the fluence at a given depth
13 other than near the perimeter of the area.

14
15 This phenomenon is best understood by reference to
16 Figures 2a and 2b.

17
18 In Figure 2a the spread of the energy present in the
19 beam, that is, the expansion of the beam due to
20 scattering, is indicated approximately by following a
21 line 30 representing the average direction of scattered
22 photons. The energy incident on the surface is within
23 an area 20 of 1mm^2 , but at a depth of 3mm 50% of the
24 incident energy can be found within a much larger area
25 21 of 1cm^2 . Thus the surface fluence is reduced by
26 about a factor of 200. (This assumes that no
27 absorption takes place.)

28
29 If a second area 22, adjacent to the first area 20 and
30 also of 1mm^2 , is illuminated with equal energy, then
31 the fluence (energy density) on the surface remains
32 constant. It can be seen from Figure 2b that at depth
33 the energy from the second source in area 23 very
34 largely overlaps that of the first source in area 21.
35 Thus the fluence at depth has almost doubled for no
36 change in surface fluence.

1 Figures 2c and 2d show the same effect but with sample
2 fluences typical of laser hair removal.

3
4 This process continues with the fraction of the surface
5 fluence effective at depth increasing with size of
6 illuminated area. The rate of increase slows to give a
7 constant fraction when the illuminated area of the
8 surface is several cm^2 . This function is sketched in
9 Figure 2e, in which line 40 shows the fluence at 3mm
10 depth (in J/cm^2) plotted against the beam diameter at
11 the surface (in mm).

12
13 The numbers used in this example are illustrative only
14 but are close to those encountered in skin. In the
15 case of hair removal, a target is approximately 3 mm
16 deep and therefore a certain level of fluence will be
17 required at that depth to achieve the required
18 therapeutic effect.

19
20 This therapeutic fluence is determined by the
21 absorption of light from lasers such as ruby and
22 alexandrite into the melanin within and around the
23 follicle. The epidermis and upper dermis, however,
24 contain the same absorbing chromophore as that present
25 in the target. Since it is desirable to spare the
26 epidermis and upper dermis from damage, and these occur
27 nearer the surface, it is clear that any means by which
28 the ratio of fluence at a depth compared with surface
29 fluence can be increased offers an improvement in
30 efficacy and safety.

31
32 An approach taught in current practice is to use large
33 areas of illumination. However this novel approach,
34 and the second aspect of the invention, is to use a
35 lens 15 to sharply focus the incident beam 3 to a point
36 16 around 3 mm below the surface 2 as shown in Figure

1 3a. Although there are many scattering events as light
2 moves through the tissue, with the consequences
3 outlined above, each event scatters light in a
4 predominantly forward direction. A sharply focused
5 beam therefore offers some counteraction to the spread
6 induced by scattering.

7
8 Unfortunately, to focus the whole beam from a pulsed
9 laser such as ruby or alexandrite presents a serious
10 safety hazard; the slightest incorrect positioning of
11 the focal point would substantially increase the
12 coherent fluence at the surface and lead to severe
13 damage.

14
15 Figure 3b shows an arrangement which overcomes this
16 disadvantage by passing the large area collimated beam
17 3 through an array 5 of small micro lenses 5a. These
18 lenses are of short focal length. The focusing
19 function of this array 5 is estimated to double the
20 sub-surface flux at point 17. There is insufficient
21 energy falling within the acceptance area of an
22 individual lens 5a to present a safety hazard.

23
24 A third aspect of the invention addresses the issue of
25 light coupling into tissue. As mentioned above, the
26 use of a gel has been suggested as a way of improving
27 light coupling. Since the tissue surface is
28 microscopically uneven, applying a gel - and thus
29 essentially smoothing the surface profile to one of
30 near normal incidence to the beam - would indeed help
31 to reduce the reflection losses associated with the
32 refractive index difference between tissue and air.
33 Unfortunately this technique does not really address
34 the reason for the 'apparent' high reflectivity of
35 tissue.

36

1 The greater portion of the apparent reflected light is
2 caused not by index mismatch but rather by transmission
3 into the tissue followed by scattering into a backward
4 direction and finally re-emergence.

5
6 Although each scattering event is predominantly in the
7 forward direction, there are, on average, some 200 such
8 events per mm penetration. As described earlier some
9 50% of the incident energy contributes to the fluence
10 at depth whilst the remaining 50% is scattered in all
11 the other directions. A half of this, that is 25% of
12 the total, actually finds its way out of the tissue,
13 contributing to the apparent reflected energy. This
14 figure of 25% is approximate and depends on the nature
15 of the tissue. In skin it can also vary between
16 individuals and on sites on the same individual.
17 However, the figure usually is between 20% and 40%.

18
19 This aspect of the invention seeks to provide means of
20 capturing this effectively reflected light by using a
21 mirror surface 6 around the handpiece 7 and thus
22 returning the light to the tissue surface 2 once more.
23 This is shown in Figure 4. The area of surface that is
24 the source of this back scattered light is larger than
25 the original illuminated area, and the emerging ray
26 directions 18 are spread widely. Under these
27 circumstances, only limited focusing of the light to be
28 returned to the tissue is possible. This is achieved
29 using a mirror surface 6 of a parabolic form. A
30 simpler hemispherical shape or a conical section are
31 alternatives which give adequate advantage.
32 Irrespective of shape, the action of returning the back
33 scattered light to the tissue surface effectively
34 provides an increase in overall coupling, and thus a
35 reduction in the applied energy required to reach a
36 therapeutic level. This reduction is estimated to be

1 around 20% and therefore an initial requirement of, for
2 example, a fluence of 20 J/cm² at the surface 2 would be
3 reduced to around 16 J/cm².

4
5 In summary, the embodiment shown in Figure 1 shows an
6 apparatus 1 incorporating a combination of the
7 improvements outlined above. This apparatus 1 includes
8 means 4 for drawing up an annulus of tissue, thereby
9 both stretching and thinning the central zone above a
10 target area. This central zone is illuminated with a
11 collimated laser beam 3 passing through an array of
12 micro lenses 5. Typically these lenses may be 1mm in
13 diameter and have a focal length of around 10mm. The
14 delivery handpiece 7 is provided with a means 6 of
15 reflecting back any scattered light returning from the
16 tissue surface.

17
18 This embodiment incorporates all the improvements
19 described. Each individual improvement, that is the
20 annular ring 4, the array of micro lenses 5 and the
21 reflector 6 may be separately applied in other simpler
22 embodiments without detracting from their individual
23 novelty.

24
25 Each individual improvement may also be combined with
26 other established methods such as tissue precooling.
27 Other techniques, for example, for stretching the skin,
28 would be included in the general principles outlined
29 here.

30
31 The embodiment described above offers significant
32 advantages to the process of hair removal with lasers
33 or other optical means. Specifically these include a
34 change in the distribution of light to increase the
35 flux density at significant depths of, for example,
36 between 1 and 3 millimetres, a reduction in the blood

1 volume in the illuminated area and an increase in the
2 effective light flux coupled to the skin. Thus
3 selectivity is improved and the optical energy from the
4 laser or other source is reduced. The embodiment shows
5 specific means for achieving these advantages.

6

7

8 Improvements and modifications may be made to the above
9 without departing from the scope of the invention.

1 CLAIMS

- 2 1. An apparatus for delivery of a beam of light to a
3 target area beneath the surface of the skin
4 comprising:
5
6 a collimated light beam source; and
7
8 light delivery means to increase the light energy
9 density at said target area while minimising the
10 light energy density at the surface of the skin.
11
- 12 2. An apparatus as claimed in Claim 1 wherein said
13 delivery means comprises a reflective surface
14 adapted to recover light reflected away from the
15 skin on incidence with the skin and to redirect
16 said reflected light towards the skin.
17
- 18 3. An apparatus as claimed in any preceding claim
19 wherein said delivery means comprises means to
20 stretch the skin above the target area.
21
- 22 4. An apparatus as claimed in Claim 3 wherein said
23 delivery means comprises means to subject an area
24 of skin adjacent to the skin above the target area
25 to vacuum suction.
26
- 27 5. An apparatus as claimed in Claim 4 wherein said
28 delivery means comprises an annular channel member
29 adapted to be sealed to the skin.
30
- 31 6. An apparatus as claimed in Claim 5 wherein said
32 channel is ring shaped or oval or of other shape.
33
- 34 7. An apparatus as claimed in Claim 5 or Claim 6
35 wherein said channel is adapted to be positioned
36 with the channel opening in contact with the skin.

- 1 8. An apparatus as claimed in any preceding claim
2 wherein said delivery means comprises means to
3 redistribute an incident collimated beam prior to
4 its incidence with the skin.
5
- 6 9. An apparatus as claimed in Claim 8 wherein said
7 redistribution means comprises an array of lenses.
8
- 9 10. An apparatus as claimed in Claim 9 wherein said
10 lenses are of short focal length.
11
- 12 11. An apparatus as claimed in Claim 9 or Claim 10
13 wherein said array is adapted to increase the flux
14 density at a predetermined depth.
15
- 16 12. An apparatus as claimed in any preceding claim
17 wherein the light beam is a laser light beam.
18
- 19 13. An apparatus as claimed in any preceding claim
20 further comprising means for precooling the tissue
21 and/or means for selective cooling of the
22 epidermis and/or devices to draw folds of skin
23 which may receive radiation from either side.
24
- 25 14. A method for delivery of a beam of light to a
26 target area beneath the surface of the skin
27 comprising the step of using an apparatus
28 according to any preceding claim.
29
- 30 15. A method for delivery of a beam of light to a
31 target area beneath the surface of the skin
32 comprising the steps of:
33
34 directing a collimated light beam onto the surface
35 of the skin; and
36

1 using a light delivery means to increase the light
2 energy density at said target area while
3 minimising the light energy density at the surface
4 of the skin.
5

6 16. A method as claimed in Claim 15 wherein a
7 reflective surface is used to recover light
8 reflected away from the skin on incidence with the
9 skin and to redirect said reflected light towards
10 the skin.
11

12 17. A method as claimed in any of Claims 15 to 16
13 wherein the skin is stretched above the target
14 area.
15

16 18. A method as claimed in Claim 17 wherein an area of
17 skin adjacent to the skin above the target area is
18 subjected to vacuum suction.
19

20 19. A method as claimed in Claim 18 wherein a vacuum
21 member comprising an inverted annular channel is
22 placed around the target area and the vacuum
23 member is evacuated to draw the skin into the
24 annular channel.
25

26 20. A method as claimed in any one of Claims 15 to 19
27 wherein said collimated light beam is passed
28 through an array of coplanar lenses positioned
29 above the skin surface.
30

31 21. A method as claimed in Claim 20 wherein said
32 lenses are microlenses of short focal length.
33

34 22. A method as claimed in Claim 20 or Claim 21
35 wherein said array is adapted to increase the flux
36 density at a predetermined depth below the skin

1 surface.

2

3 23. A method as claimed in Claim 22 wherein said
4 predetermined depth is between 1 and 5 mm,
5 preferably between 2 and 4 mm.

6

7 24. A method as claimed in any one of Claims 15 to 23
8 wherein the light beam is a laser light beam.

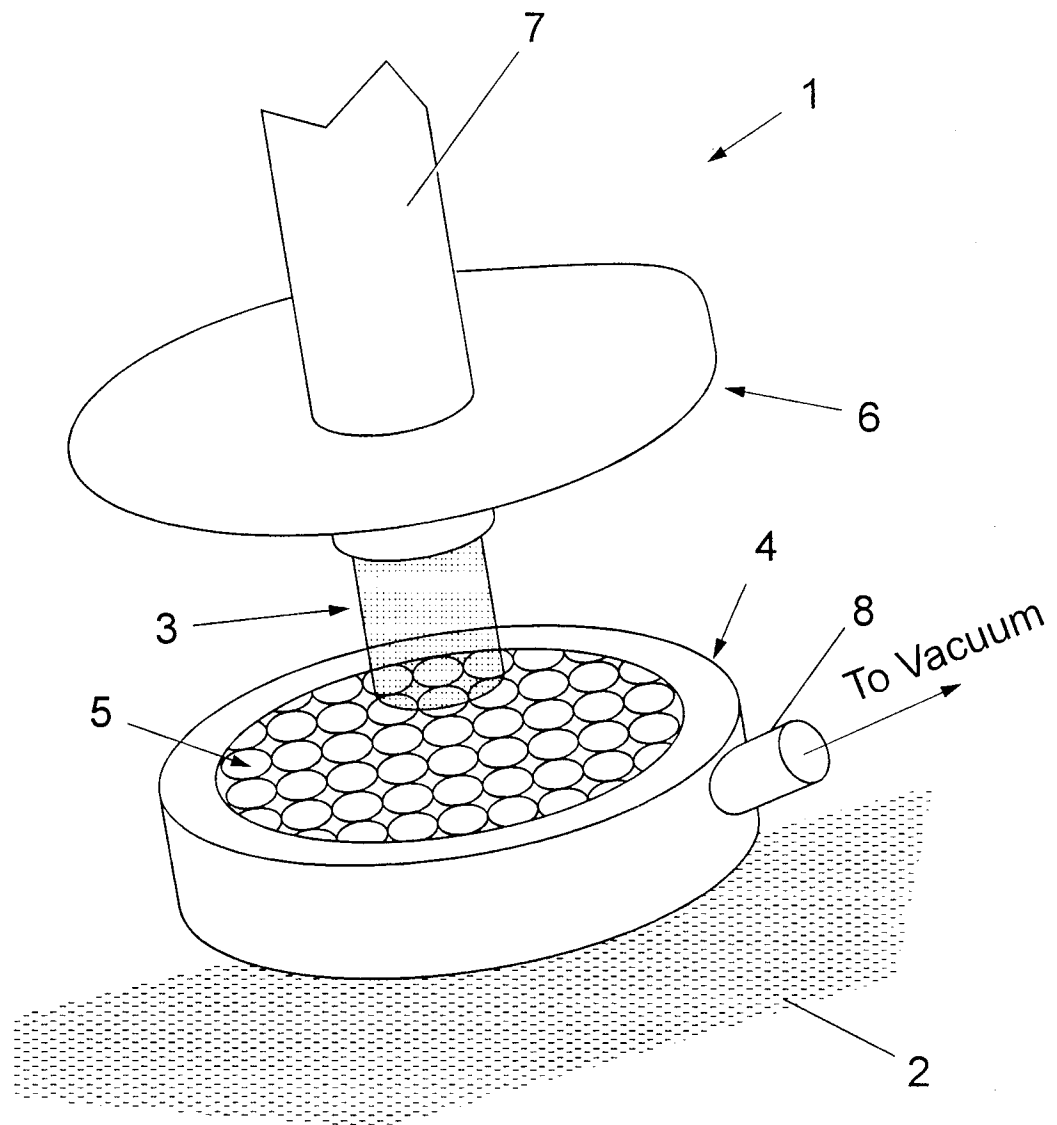
9

10 25. A method as claimed in any preceding claim further
11 comprising the steps of precooling the tissue
12 and/or selective cooling of the epidermis and/or
13 use of optical transmitting gels and/or use of
14 convex shaped applicators and/or use of devices to
15 draw folds of skin which may receive radiation
16 from either side.

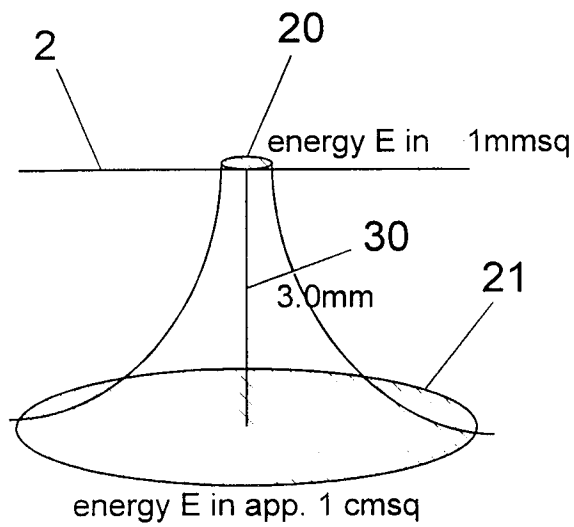
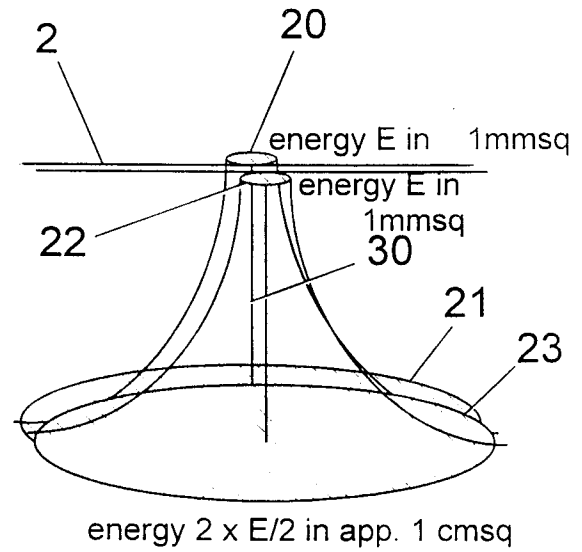
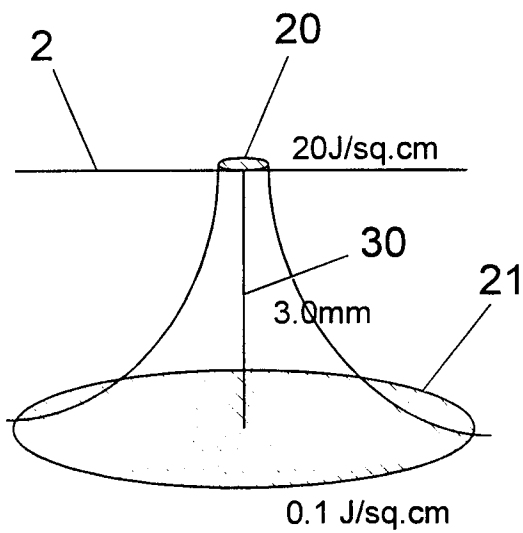
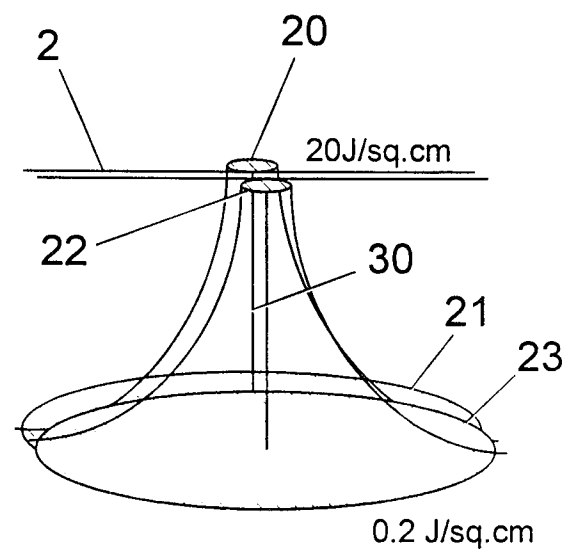
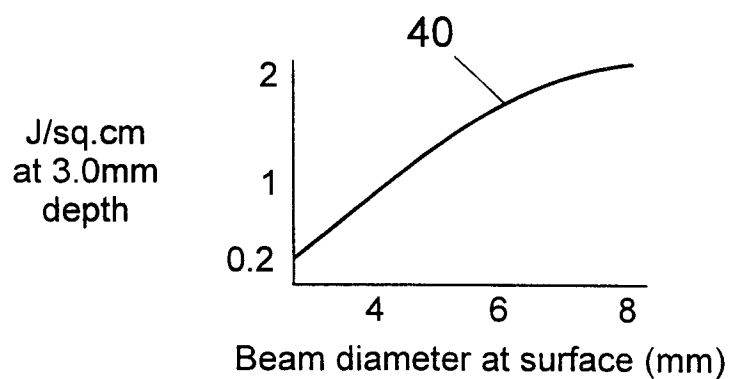
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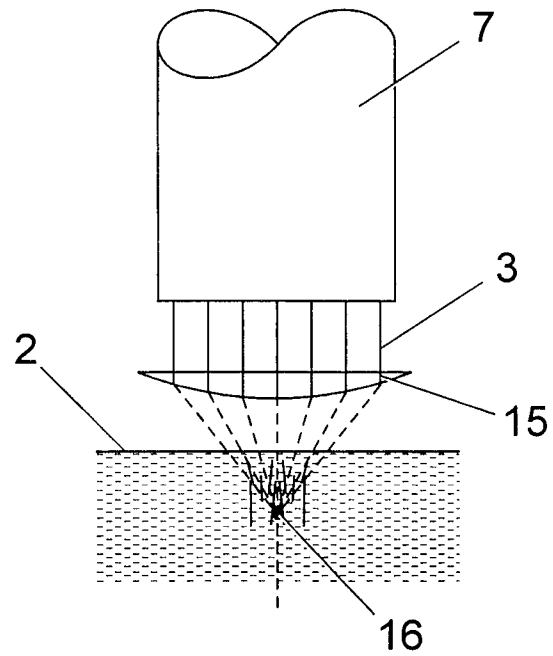
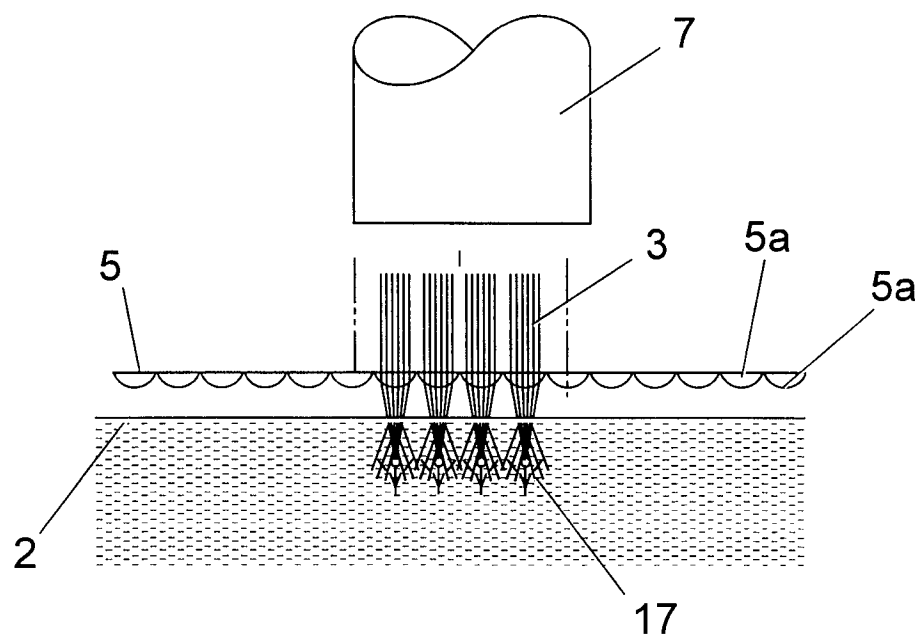
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*Fig. 1*

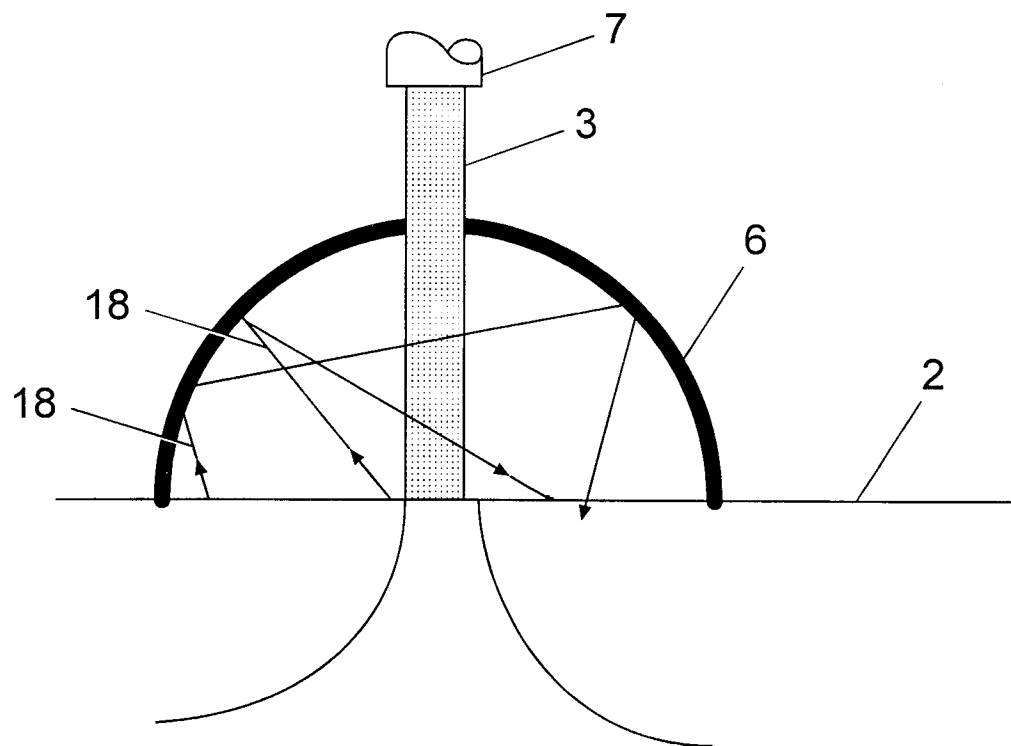
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*Fig. 2a**Fig. 2b**Fig. 2c**Fig. 2d**Fig. 2e*

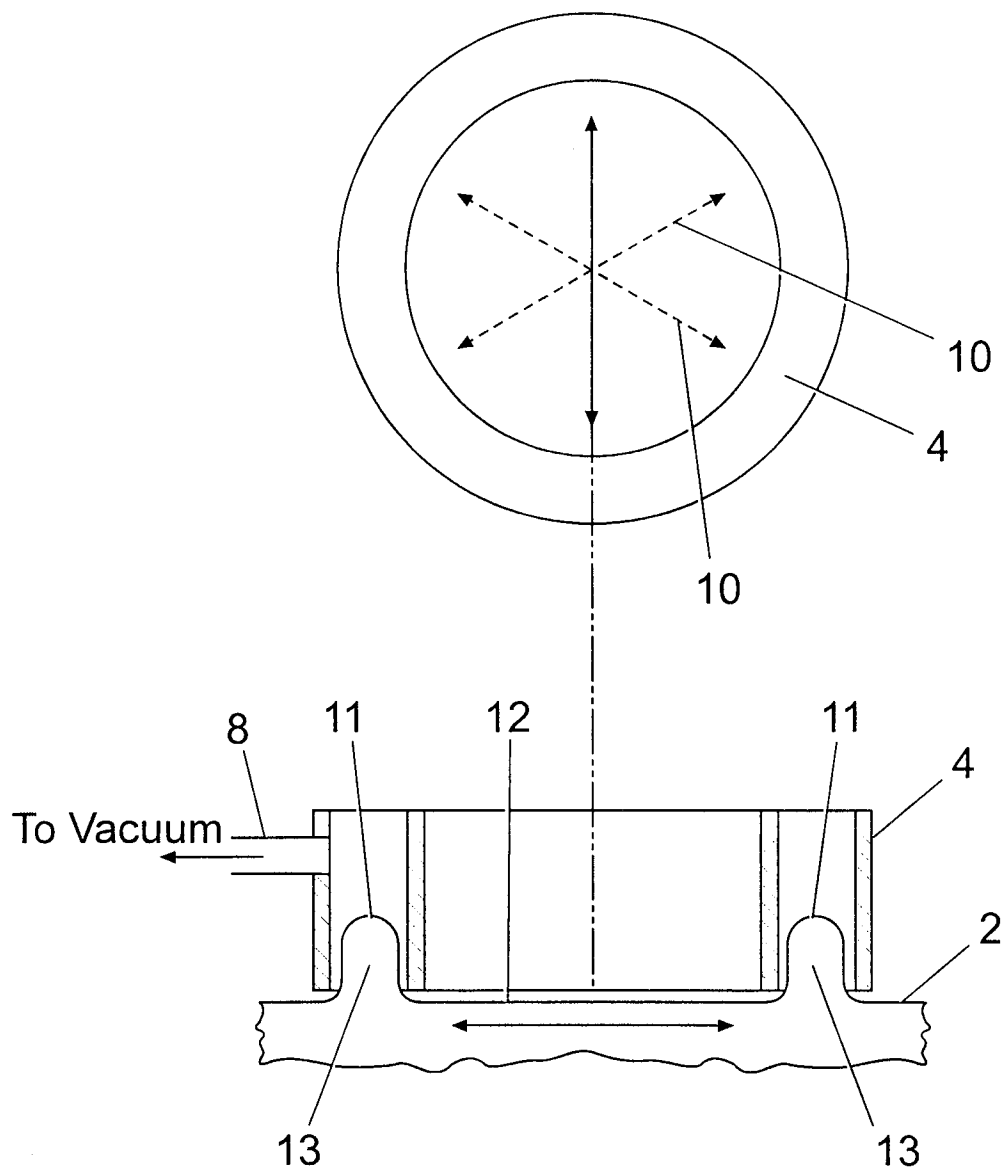
3 / 5

*Fig. 3a**Fig. 3b*

4 / 5

*Fig. 4*

5 / 5

*Fig. 5*

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 98/01523

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 A61B17/41

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61B A61N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 595 568 A (ANDERSON) 21 January 1997 see abstract see column 4, line 50 - column 5, line 32 see column 4, line 50 - column 5, line 32 see column 5, line 63 - column 6, line 21 see column 6, line 42 - line 56 ---	1-3,12, 13
X	US 5 546 214 A (BLACK) 13 August 1996 see abstract ---	1,2
X	WO 84 02644 A (WEISSMAN) 19 July 1984 see abstract ---	1
	-/--	



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

° Special categories of cited documents :

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T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

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Date of the actual completion of the international search

30 July 1998

Date of mailing of the international search report

05.08.98

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 98/01523

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	US 5 735 844 A (ANDERSON) 7 April 1998 see abstract; figures 2A,2B,3B see column 2, line 6 - line 47 see column 5, line 21 - column 6, line 36 see column 14, line 5 - line 67 ---	1-13
P,X	US 5 653 706 A (ZAVISLAN) 5 August 1997 see abstract see column 1, line 31 - line 52 -----	1-3

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 98/01523

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 14-25
because they relate to subject matter not required to be searched by this Authority, namely:
Rule 39.1(4)
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 98/01523

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
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			CN	1172420 A	04-02-1998
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			JP	9501334 T	10-02-1997
			WO	9503089 A	02-02-1995



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(21) International Application Number: PCT/US98/20988 (22) International Filing Date: 6 October 1998 (06.10.98) (30) Priority Data: 08/947,364 8 October 1997 (08.10.97) US (71) Applicant: TRIMEDYNE, INC. [US/US]; 2801 Barranca Road, P.O. Box 57001, Irvine, CA 92714-7001 (US). (72) Inventor: CONE, Robert, Roy; 18672 Florida Street, Huntington Beach, CA 92648-1925 (US). (74) Agents: CEPURITIS, Talivaldis et al.; Olson & Hierl, Ltd., 36th floor, 20 North Wacker Drive, Chicago, IL 60606 (US).		(81) Designated States: DE, IL, JP. Published <i>With international search report.</i>
(54) Title: PERCUTANEOUS LASER TREATMENT (57) Abstract <p>A method of percutaneous and subcutaneous laser treatment of the tissue of a patient is provided. The tip of an optical fiber is passed through the skin, advanced through the tissue subcutaneously to a desired treatment area and withdrawn. Laser energy can be emitted at different levels during any or all of the skin penetration, advancement, tissue treatment and withdrawal phases. The present invention is useful for surgical treatments, and is especially suitable for minimally invasive plastic or cosmetic surgical and dermatological procedures without bleeding and with less edema, erythema and swelling and faster healing than conventional surface laser energy application, abrasion, scalpel surgery or chemical peel procedures.</p>		

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PERCUTANEOUS LASER TREATMENT

TECHNICAL FIELD

The present invention relates to methods and procedures for the amelioration of cosmetic flaws and the like by the application of laser energy to a selected target region or site. The present invention is useful in the practice of surgery, especially plastic and cosmetic surgery, as well as dermatology. The present invention is especially suitable for minimally invasive surgical treatments in which a percutaneous approach is desired.

BACKGROUND OF THE INVENTION

Biological tissue comprises cells embedded in a primarily proteinaceous extracellular matrix. Collagen is one of the predominant proteins found in the extracellular matrix. Collagen can be altered by the application of thermal energy to become denatured and act as a biological glue. Thermal energy can also cause collagen fibers to become cross-linked, reducing the volume of the thermally treated collagen. The thermal effect may be conveniently produced by the interaction of laser generated light energy with tissue. Laser energy of the appropriate wavelength, energy and geometry can thus be used to weld together opposed tissue surfaces and shrink collagen-containing tissues.

The use of laser devices in various types of surgery is known. Such devices cause thermal coagulation and/or ablation of tissue by emission of a predetermined level of laser energy for a predetermined time. The unwanted tissue can be coagulated to the desired depth by laser energy at low energy density, or ablated by subjecting the tissue to a higher level of energy density. However, when laser energy is applied to the skin from an external source, erythema or sun-burning frequently occurs. The erythema can take weeks or months to subside, and discoloration or scarring of the skin may be a lasting result.

Several plastic surgery procedures involve the surgical removal of subcutaneous fat and excess skin and the tightening of the remaining skin. Such procedures include meloplasty (face lifts), eyebrow lifts and blepharoplasty for removal of bags under the eyes (dermochalasis and blepharochalasis). Beyer, C.K., Baggy lids, Int. Ophthalmol. Clin., **10**: 47-53 (1970). Traditional surgical approaches require cutting and removing excess skin and fat using incisions often centimeters in length. These approaches are subject to potential complications such as hemorrhage, hematoma, infection and removal of too much skin or fat

(overcorrection). Kohn, R., Textbook of Ophthalmic Plastic and Reconstructive Surgery, pp. 177-191, 186, Lea & Febiger, Philadelphia (1988). As an example, surgical procedures for blepharoplasty are complex. Inappropriate or poorly performed surgery may result in an adverse cosmetic result, or may place the patient at risk for developing vision-threatening complications. Custer, P.L., Lower eyelid blepharoplasty, in Bosniak, S., editor, Principles and Practice of Ophthalmic Plastic and Reconstructive Surgery, pp. 617-625, 624, W.B. Saunders, Philadelphia (1996).

Lasers have been employed in cosmetic and reconstructive surgery. The Nd:YAG laser has been used to make incisions in the skin for face lifts (meloplasty) and for removal of bags under the eyes by blepharoplasty. Apfelberg, D.B., YAG laser meloplasty and blepharoplasty, Aesth. Plast. Surg. **19**: 231-235 (1995). However, the Nd:YAG laser's continuous wave energy may be overly thermal and cause an excessively deep zone of penetration (about 4000 μ m). The CO₂ laser has been employed in blepharoplasty using the transconjunctival approach. David, L.M., The laser approach to blepharoplasty, J. Dermatol. Surg. Oncol. **14**: 741-235 (1988). While the use of laser energy has been reported to reduce bleeding during surgery and reduce pain during healing, a large incision is still required. Morrow, D.M., and Morrow, L.B., CO₂ laser blepharoplasty. A comparison with cold-steel surgery, J. Dermatol. Surg. Oncol., **18**: 307-313 (1992). The only advantage provided by the described laser technique was less swelling after surgery.

What is needed is a method of plastic surgery using a laser that provides more desirable tissue effects and which can also be used in a minimally invasive percutaneous approach.

SUMMARY OF THE INVENTION

A percutaneous method for the treatment of skin and subcutaneous tissue by means of a laser device capable of emitting pulses of light energy of an appropriate wavelength with relatively short pulse widths, at relatively low energy per pulse and relatively rapid pulse repetition rates is provided by the present invention. Light energy characterized by such parameters is applied subcutaneously to tissues underlying the skin. The method is useful for the practice of surgery, especially plastic and cosmetic surgery as well as dermatology. The method is non-invasive or minimally invasive and well suited for outpatient therapy. In particular, application of the laser energy directly to the tissue beneath the skin eliminates or

reduces the erythema that can result when laser energy is applied to the skin from outside the body.

The method of the present invention is especially suitable for several procedures used in plastic and cosmetic surgery as well as dermatology. Procedures for which the method of the present invention can be used include, inter alia, the removal of pigmentation, such as lentigines (age spots), hyperpigmentation, lentigo (freckles), café-au-lait macules, actinic keratosis, melasma, and tattoos (body or facial). The method of the present invention can also be used for the removal of plantar warts, chin reshaping via the percutaneous laser melting or desiccation of fat, amelioration of turkey neck, and the treatment of some dilated blood vessels associated with rosacea. The method of the present invention is also suitable for coagulation of spider veins (< 1 mm), removal of keloid scars, coagulation of varicose veins (> 1 mm), reshaping of the upper lip, reshaping of the eyelids, permanent ablation of the hair follicle to permanently prevent hair regrowth and some types of otoplasty. The method of the present invention is also suitably used for the treatment of various cutaneous vascular lesions, such as port wine stains, hemangiomas, and telangiectasias, including those of the face and the leg.

The method of the present invention can also be used for plastic surgery treatments such as skin resurfacing, removal of perioral, periorbital and ear lobe wrinkles, treatment of nasal labial folds, perioral fat pads and marionette lines, lip lift, neck lift, eyebrow lift, lipolysis (of upper and lower eyelids, cheeks, abdomen, thighs), blepharoplasty, rhinoplasty, treatment of polly beak and internal weir (nostril reduction). Scars that can be treated using the method of the present invention include acne scars, keloids, chicken pox scars, stretch marks (striae), hypertrophic scars, and skin graft hypertrophy as well as pits and depressions. In addition, the method of the present invention is also suitable for burn debridement, and for the treatment of corns, papilloma (warts, condylomas, polyps) and skin cancer, including basal cell carcinoma.

A pulsed or continuous wave holmium:YAG laser, holmium:YSGG laser or other laser emitting light energy at a wavelength of about 1800 micrometers to about 2200 micrometers ("holmium laser") may be converted, in accordance with the present invention, to produce pulses of variable pulse-width at various energy levels. The light energy from a holmium laser has an ideal depth of penetration into tissue, about 250 to 400 μm . The holmium laser is a preferred light energy source

because light energy obtained therefrom has the property of being able to cause cross-linking of collagen proteins, lysis of fat and bloodless incisions, primarily due to the wavelength of light emitted.

Energy from a relatively low power, short pulse-width, high
5 repetition rate holmium laser, applied percutaneously through an optical fiber, can avoid burning or charring the tissue while accomplishing the desired beneficial physiologic effect. At lower energy densities, the collagen component of tissue can be cross linked, reducing its volume and causing shrinkage of the tissue. The
10 holmium laser preferred for the practice of the present invention provides a marked advantage over earlier surgical techniques. Benefits of the holmium laser include less postoperative swelling, faster healing, no bleeding and no sutures to be removed. Additionally, the method of the present invention allows for the melting or desiccation of subcutaneous fat by the use of a relatively small diameter optical fiber, e.g. a 25-400 μm core diameter, that is introduced through the skin. The small
15 diameter of the optical fiber, coupled with the low energy used, typically about 3 to 100 millijoules per pulse (mJ/pulse), the narrow pulse-width, typically less than 100 microseconds (μs), and relatively fast repetition rate, generally 20 to 80 pulses per second (Hz), allow the fiber to penetrate the skin and be used subcutaneously upon tissue without perceptible charring as a result. Preferably, an energy level of about 3
20 mJ/pulse to about 20 mJ/pulse is used while the tip of the optical fiber is inserted through the skin. In comparison, most holmium lasers currently used in surgery are not stable in producing less than 500 mJ/pulse, typically have a pulse width of 300 to 350 μs and a repetition rate of 1 to 25 Hz.

The laser source typically comprises a housing containing the laser
25 generating unit as well as optical and electronic control components therefor. The optical fiber is connected proximally to the light output of the laser and extends distally through a hand piece held by the surgeon. The light energy produced by the laser source is introduced into the proximal end portion of the optical fiber, which itself passes through a handpiece, and is emitted from the bare distal tip of the optical
30 fiber distally to the target tissue. The tip of the optical fiber preferably has a core diameter of about 25 μm to 400 μm , more preferably about 50 μm to about 200 μm .

The face of the optical fiber tip is preferably aligned at a right angle to its longitudinal axis. Bleeding at the entry and exit point may be minimized by lasing at extremely low energy, as low as 1 mJ/pulse with a very short pulse width,

preferably 10-30 μ S, during insertion through the skin or withdrawal of the optical fiber from the treatment site while exiting the skin.

The method aspect of the present invention includes a subcutaneous advancement phase as well as a withdrawal phase. In use, after penetration of the skin as described above, the tip of the optical fiber is moved forwardly through the tissue during the advancement phase. During this phase, the tip of the optical fiber is advanced through the tissue for the desired distance without emission of laser energy or with laser emission at a controlled power level chosen to achieve the effect desired. If desired, laser energy can be emitted from the tip during the advancement phase at a controlled energy level of less than about 3 to about 20 mJ/pulse, at a frequency of 20 to 80 Hz and a pulse width of 30 to 100 μ S. A preferred energy emission frequency during the advancement phase is about 20 to 60 Hz. During advancement, very low emission energy of 3-10 mJ/pulse can be used to facilitate the advancement of the optical fiber and prevent tissue adherence to the optical fiber. If desired, laser energy to obtain a desired therapeutic effect can be emitted at an energy of 5 to 50 mJ/pulse.

The tip of the optical fiber may be maintained at the position of furthest advance and laser energy emitted there, or alternatively, the tip may be immediately withdrawn. During the period while the tip of the laser probe is being used to treat the tissue at a selected site, laser energy can be emitted at an energy of about 5 to about 50 mJ per pulse at a frequency of about 20 to about 60 Hz. During the withdrawal phase, laser energy can be emitted at about 5 to about 50 mJ/pulse at a frequency of about 20 to about 60 Hz, depending on the tissue effect desired, or at about 3 to about 10 mJ/pulse to prevent tissue adhering to the fiber during withdrawal. In other cases, the fiber can be withdrawn without using laser energy. The energy level can also be changed as the fiber moves from one area to another under the skin to obtain a desired effect. It is not necessary to remove the optical fiber, or to turn off the laser while the surgery is being performed.

In general, the level of light energy emitted during the withdrawal phase is equal to or greater than the emission level, if any, during the advancement phase. The power output, frequency and pulse-width may be varied as required to achieve the desired result, based on the surgeon's clinical experience.

DETAILED DESCRIPTION OF THE INVENTION

The method of the present invention initially produces a subcutaneous tunnel or cavity through the tissue as the tip of the optical fiber is moved forwardly during the advancement stage, or rearwardly during the withdrawal stage, usually while emitting light energy at a relatively low energy level and a relatively short pulse width. However, in some cases, for example, if extremely thin skin could be damaged by emitting light energy during advancement or withdrawal, the tip of the optical fiber can be advanced or withdrawn without emitting light energy.

10 The selected area can be treated by repeated advancement and withdrawal cycles of the tip of the optical fiber as appropriate. Each cycle can be directed at the same or a different radial angle. However, to avoid damage to blood vessels which can be situated substantially normal to the skin's surface, the optical fiber is moved unidirectionally rather than so as to sweep laterally through a sector like a windshield wiper. Advancement and withdrawal cycles are repeated as appropriate through other openings within the selected region, until the entire region has been treated.

Tissue can be removed or affected by several processes, including vaporization; cross linkage, which produces shrinkage; disruption of cellular membranes; desiccation of fat cells; lipolysis or melting of fat cells; melting and fusion of tissue components (welding) and denaturation or coagulation of proteins. Little bleeding occurs during such processes due to the hemostasis produced by the effects of the applied light energy. The effects produced depend on the wavelength and energy level used. The process of tissue ablation requires relatively higher energy levels. Tissue welding may be used to join opposed tissue surfaces at relatively low energy levels, without the need for sutures and their subsequent removal.

Blood and tissue coagulation is produced by heating the tissue to at least about 62 degrees Celsius. Tissue vaporization or ablation is produced by heating the tissue to at least about 100 degrees Celsius, causing the water in the cells to turn into steam. The small volume of steam produced is rapidly cooled by interaction with the tissue, and quickly condenses. Tissue disruption may also be caused by attendant concurrent acoustic effects of laser energy emission.

The physiological response of the treated area progresses through a continuum of at least three phases of wound healing after superficial or percutaneous laser treatment. First, there is an edema phase, seen in many cases within about 10 days after treatment. The sequence of events generally follows a course including

5 two days of swelling and two days of subsidence. Usually swelling is less pronounced after treatment with a holmium laser than after treatment with a CO₂ laser. The second phase is characterized by the proliferation of fibroblasts. The third phase is the resolution phase in which tissue remodeling takes place.

The tissue in the region to be treated subcutaneously is preferably

10 hydrated before laser treatment by the injection of water or an aqueous saline solution. The water or aqueous saline solution used for this purpose may include an acceptable local anesthetic. The overall treatment parameters of energy levels, pulse width and frequency typically used in illustrative procedures are tabulated in Table 1, below.

15 In each case, for penetration of the skin, the optical fiber was positioned perpendicular to the skin, and a very low level of light energy was emitted while very gentle pressure was applied. Typical parameters used for skin penetration were 3-10 mJ/pulse, preferably about 5 mJ/pulse, frequency of about 20-60 Hz and pulse width of about 40-80 μ S, although skin penetration of the fiber optic can also

20 be achieved using lower or higher energies.

Similar energy parameters may be used to prevent or minimize tissue adherence while advancing the fiber to the treatment site or withdrawing the fiber from the treatment site. The preferred energy parameters for treatment at the site or along a tissue track, are set forth in Table 1.

TABLE 1
Preferred Parameters for Holmium Laser Treatment
in Selected Procedures

	PROCEDURE	FREQUENCY Hz	ENERGY mJ/Pulse	PULSE WIDTH (μ S)
5	Upper Blepharoplasty	20-60	5-40	50-80
	Lower Blepharoplasty	20-60	5-40	40-70
	Vein Coagulation	20-60	5-40	70-90
	Skin Wrinkle Removal	20-60	5-40	40-70
10	Telangiectasia	20-60	5-20	40-100

The laser tissue effect on the selected tissue site can be controlled by modulating the energy per pulse, repetition rate and/or pulse width of the emitted laser energy.

15

EXAMPLE 1

PERCUTANEOUS LOCALIZED

TREATMENT PARALLEL TO THE SKIN SURFACE

The areas selected for treatment were first hydrated by an injection of water, an aqueous saline solution, or, preferably, an aqueous saline solution containing an appropriate local anesthetic. The injected liquid served to absorb excess light energy and heat to cool the tissue, and to provide a buffer zone, which is especially useful in some locations, such as around the eyes.

The tip of the optical fiber was placed on the skin surface, at about a 90 degree angle to the skin surface. The optical fiber was a bare optical fiber of about 100 μ m to about 365 μ m in core diameter, preferably about 200 μ m core diameter. The tip pierced the skin and was advanced into the subcutaneous tissue while emitting laser energy at about 5 mJ/pulse, a pulse width of about 40 to about 70 μ S at a frequency of about 20 to about 60 Hz. Low energies were used to minimize adverse thermal effects to the skin, such as scarring, depigmentation or hyperpigmentation, at the site of entry.

After insertion of the tip of the optical fiber through the skin, the fiber was turned so that it was roughly parallel to the plane of the skin surface. The fiber was advanced and withdrawn repeatedly as needed to treat the selected region.

Energy emission was increased after the initial advancement stage to a therapeutic level of about 5 to about 50 mJ/pulse, depending on the diameter of the fiber, smaller fibers requiring less energy. Preferably, about 20 mJ/pulse was used at about the same pulse width and frequency. The optical fiber was moved axially to and from, but not swept laterally like a windshield wiper. The treatment of a selected area continued until audible cavitation sounds ("popping") ceased. Such cavitation sounds signalled the destruction of the fat present at the site (lipolysis) and the heating of the collagen. The optical fiber was then withdrawn from the skin, while continuing to emit energy at or below the therapeutic level, in order to minimize the amount of tissue adhering to the tip of the optical fiber.

This method has been used when the primary objective is the removal of fat or the coagulation of blood vessels, with a secondary objective of tightening the skin. This method is appropriate, for example, for lipolysis of the fat pads and tightening (blepharoplasty) of the upper and lower eyelids, removal of nasal labial folds, removal of perioral and periorbital wrinkles; treatment of marionette lines and wrinkles of the ear lobes; neck lifts and lip lifts. This method may also be used for coagulation of telangiectasias, varicose and spider veins, hemangiomas and rosacea.

20

EXAMPLE 2

PERCUTANEOUS LOCALIZED

TREATMENT NON-PARALLEL TO SKIN SURFACE

The method of Example 1 was used with the modification that the optical fiber was directed to the treatment site or used along a treatment track that was not parallel to the plane of the skin surface. This method is appropriate, for example, for the treatment of polly beak, wherein the shape of the nose is lifted and reshaped as desired by producing tissue shrinkage combined with lipolysis. For this purpose, the frequency used was about 20 to about 60 Hz; all other parameters were the same as used in Example 1. This method is useful when the primary objective is the removal of fat or removal of excess vascularization, with a secondary objective of tissue shrinkage to tighten the skin.

EXAMPLE 3

TATTOO REMOVAL

Tattoo removal is accomplished by inserting the tip of the optical fiber through the skin in the pigmented area, at the fiber penetration energy parameters as described above, keeping the optical fiber perpendicular to the skin or tilting it at an angle substantially parallel to the skin and advancing and withdrawing the optical fiber while emitting energy at the parameters as described in Example 1. Subsequent additional penetrations are made until the entire pigmented area is treated.

EXAMPLE 4

INCISION (INTERNAL WEIR)

A bare optical fiber about 365 μm in diameter was inserted at the base of the nostril. The method of Example 1 was used to create a wedge-shaped opening or channel; the parameters were: about 10 to about 50 mJ/pulse, preferably about 20 mJ/pulse, pulse width 50-70 μs and frequency about 60 Hz. The edges of the channel were sutured together to reduce the size of the nostril opening.

EXAMPLE 5

CARTILAGE VAPORIZATION, BONE REDUCTION

This method is useful for rhinoplasty (commonly referred to as a nose job), which can be performed without postoperative bruising and black eyes. A series of holes are made through the skin and through cartilaginous and bony tissue using the optical fiber. The holes are placed at or around the nose ridge protrusion in a configuration like the perforations at the edges of a postage stamp. During the entry phase, the tip of the 200 or 365 μm bare optical fiber is placed at a 90 degree angle relative to the skin. Low energies (about 5 mJ/pulse), are used to minimize adverse thermal effects on the skin at the entrance point of the optical fiber.

Therapy is administered by advancing the fiber internally through cartilaginous and/or bony tissue. Energy parameters for therapy are 15-40 mJ/pulse, 40-70 μs pulse width, at 20-60 Hz. After the "postage stamp" configuration is completed, external pressure is applied to the "postage stamp" to dislocate it from its original structural connections. The cartilaginous/bone fragment may be left in the body to be naturally absorbed over time.

EXAMPLE 6COAGULATION OF VARICOSE VEINS

This method is useful for treatment of varicose veins. The area surrounding the veins to be treated was anesthetized. The optical fiber, preferably a
5 bare optical fiber, about 200 μm to about 365 μm in diameter, was placed on the skin above one end of the visible portion of the vein to be treated. The optical fiber penetrated the surface of skin at about a 90 degree angle and entered the vein, using parameters of about 5 mJ/pulse, 50-90 μS pulse width and 20-60 Hz. The energy was increased to about 5-25 mJ/pulse, preferably about 15 mJ/pulse, with the optical
10 fiber tip within the vein. Treatment was continued until the vein was coagulated. After the treatment, the tip of the optical fiber was withdrawn while lasing at the therapeutic parameters, i.e. about 5-25 mJ/pulse, preferably about 15 mJ/pulse, 50-90 μS pulse width and 20-60 Hz. The treatment was repeated at the other end of the visible portion of the varicose vein.

15 The foregoing is intended to be illustrative of the present invention, but not limiting. Numerous variations and modifications of treatment parameters and energy sources may be utilized without departing from the spirit and scope of this invention.

CLAIMS:

1. A method for percutaneous laser treatment of a patient having a condition requiring treatment, comprising the steps of:
selecting the area to be treated;
5 selecting a source of holmium laser energy;
selecting an optical fiber of appropriate core diameter;
inserting the tip of the optical fiber through the patient's skin into tissue;
advancing the tip of the optical fiber through tissue;
10 treating the tissue;
withdrawing the tip of the optical fiber through the tissue; and
emitting the holmium laser energy through the tip of the optical fiber at an energy level less than about 200 millijoules per pulse, with a pulse width less than about 200 microseconds and at an energy emission frequency of greater than
15 about 5 Hertz while treating the tissue.
2. The method of claim 1, further comprising the step of emitting the holmium laser energy through the tip of the optical fiber at an energy level less than about 200 millijoules per pulse, with a pulse width less than about 200 microseconds and at an energy emission frequency of greater than about 5 Hertz
20 while advancing the tip of the optical fiber.
3. The method of claim 1, further comprising the step of emitting the holmium laser energy through the tip of the optical fiber at an energy level less than about 200 millijoules per pulse, with a pulse width less than about 200 microseconds and at an energy emission frequency of greater than about 5 Hertz
25 while withdrawing the tip of the optical fiber.
4. The method of claim 2 wherein the pulsed holmium laser energy is emitted through the tip of the optical fiber at a selected energy level less than about 100 millijoules per pulse, with a pulse width less than 100 microseconds and at an energy emission frequency greater than about 20 Hertz while the tip of the
30 optical fiber is advanced through the tissue.
5. The method of claim 1 further comprising the step of emitting light energy from the tip of the optical fiber while the tip of the optical fiber is inserted through the skin at an energy level of about 3 millijoules per pulse to about 20 millijoules per pulse.

6. The method of claim 1 wherein the energy emission level while the tip of the optical fiber is advanced through the tissue is about 3 milliJoules per pulse to about 20 milliJoules per pulse.
7. The method of claim 2 wherein the energy emission
5 frequency while the tip of the optical fiber is advanced through tissue is about 20 to 80 Hertz.
8. The method of claim 5 wherein the energy emission frequency while the tip of the optical fiber is inserted through the skin is about 20 to 80 Hertz.
9. The method of claim 2 wherein the energy emission level
10 while the tip of the optical fiber is advanced through tissue is about 5 milliJoules per pulse to about 50 milliJoules per pulse.
10. The method of claim 3 wherein the energy emission level while the tip of the optical fiber is withdrawn through tissue is about 5 milliJoules per
15 pulse to about 50 milliJoules per pulse.
11. The method of claim 2 wherein the energy emission frequency while the tip of the optical fiber is advanced through tissue is about 20 to about 80 Hertz.
12. The method of claim 3 wherein the energy emission
20 frequency while the tip of the optical fiber is withdrawn through tissue is about 20 to about 80 Hertz.
13. The method of claim 1 wherein the pulse width is 5 to 100 microseconds.
14. The method of claim 1 wherein the tissue is skin tissue.
15. The method of claim 1 wherein the tissue is tissue underlying
25 the skin.
16. The method of claim 1 wherein the condition requiring treatment is blepharochalasis.
17. The method of claim 1 wherein the condition requiring
30 treatment is dermochalasis.
18. The method of claim 1 wherein the condition requiring treatment is turkey neck.
19. The method of claim 1 wherein the condition requiring treatment is rosacea.

20. The method of claim 1 wherein the condition requiring treatment is plantar warts.

21. The method of claim 1 wherein the condition requiring treatment is keloid scars.

5 22. The method of claim 1 wherein the condition requiring treatment is telangiectasia.

23. The method of claim 1 wherein the condition requiring treatment is wrinkles.

10 24. The method of claim 1 wherein the condition to be treated is unwanted hair follicles.

25. The method of claim 1 wherein the condition to be treated is the pigmented area of a tattoo.

26. The method of claim 1 wherein the condition requiring treatment is marionette lines.

15 27. The method of claim 1 wherein the condition requiring treatment is basal cell carcinoma.

28. The method of claim 1 wherein the condition requiring treatment is acne scars.

20 29. The method of claim 1 wherein the condition requiring treatment is chicken pox scars.

30. The method of claim 1 wherein the condition requiring treatment is age spots.

31. The method of claim 1 wherein the condition requiring treatment is hemangioma.

25 32. The method of claim 1 wherein the condition requiring treatment is port wine stains.

33. The method of claim 1 wherein the condition requiring treatment is hyperpigmentation.

30 34. The method of claim 1 wherein the condition requiring treatment is varicose veins.

35. The method of claim 1 wherein the condition requiring treatment is polly beak.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/20988

A. CLASSIFICATION OF SUBJECT MATTER

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US CL : 606/9, 15

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 606/7, 9-17

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

APS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,000,752 A (HOSKIN et al) 19 March 1991.	1-35
Y	US 5,578,029 A (TRELLES et al) 26 November 1996.	1-35
A, E	US 5,830,208 A (MULLER) 03 November 1998.	1-35

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
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(21) International Application Number: PCT/US98/21040 (22) International Filing Date: 6 October 1998 (06.10.98) (30) Priority Data: 08/947,362 8 October 1997 (08.10.97) US (71) Applicant: TRIMEDYNE, INC. [US/US]; 2801 Barranca Road, P.O. Box 57001, Irvine, CA 92714-7001 (US). (72) Inventors: LOEB, Marvin, P.; Apartment 101, 2872 Coast Circle, Huntington Beach, CA 92649 (US). DAMASCO, Sanford; 4838 Bentree Avenue, Long Beach, CA 90807 (US). (74) Agents: CEPURITIS, Talivaldis et al.; Olson & Hierl, Ltd., 36th floor, 20 North Wacker Drive, Chicago, IL 60606 (US).		(81) Designated States: DE, IL, JP. Published <i>With international search report.</i>
(54) Title: PERCUTANEOUS LASER TREATMENT (57) Abstract A method of percutaneous and subcutaneous laser treatment of the tissue of a patient is provided. The tip of an optical fiber is to be passed through the skin, advanced through the tissue subcutaneously to a desired treatment area and withdrawn. Laser energy can be emitted at different levels during any or all of the skin penetration, advancement, tissue treatment and withdrawal phases. The present invention is useful for surgical treatments, and is especially suitable for minimally invasive plastic or cosmetic surgical and dermatological procedures without bleeding and with less edema, erythema and swelling and faster healing than conventional surface laser energy application, abrasion, scalpel surgery or chemical peel procedures.		

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PERCUTANEOUS LASER TREATMENT

TECHNICAL FIELD

The present invention relates to methods and procedures for the amelioration of cosmetic flaws and the like by the application of laser energy to a selected target region or site. The present invention is useful in the practice of surgery, especially plastic and cosmetic surgery, as well as dermatology. The present invention is especially suitable for minimally invasive surgical treatments in which a percutaneous approach is desired.

BACKGROUND OF THE INVENTION

Biological tissue comprises cells embedded in a primarily proteinaceous extracellular matrix. Collagen is one of the predominant proteins found in the extracellular matrix. Collagen can be altered by the application of thermal energy to become denatured and act as a biological glue. Thermal energy can also cause collagen fibers to become cross-linked, reducing the volume of the thermally treated collagen. The thermal effect may be conveniently produced by the interaction of laser generated light energy with tissue. Laser energy of the appropriate wavelength, energy and geometry can thus be used to weld together opposed tissue surfaces and shrink collagen-containing tissues.

The use of laser devices in various types of surgery is known. Such devices cause thermal coagulation and/or ablation of tissue by emission of a predetermined level of laser energy for a predetermined time. The unwanted tissue can be coagulated to the desired depth by laser energy at low energy density, or ablated by subjecting the tissue to a higher level of energy density. However, when laser energy is applied to the skin from an external source, erythema or sun-burning frequently occurs. The erythema can take weeks or months to subside, and discoloration or scarring of the skin may be a lasting result.

Several plastic surgery procedures involve the surgical removal of subcutaneous fat and excess skin and the tightening of the remaining skin. Such procedures include meloplasty (face lifts), eyebrow lifts and blepharoplasty for removal of bags under the eyes (dermochalasis and blepharochalasis). Beyer, C.K., Baggy lids, Int. Ophthalmol. Clin., **10**: 47-53 (1970). Traditional surgical approaches require cutting and removing excess skin and fat using incisions often centimeters in length. These approaches are subject to potential complications such

as hemorrhage, hematoma, infection and removal of too much skin or fat (overcorrection). Kohn, R., Textbook of Ophthalmic Plastic and Reconstructive Surgery, pp. 177-191, 186, Lea & Febiger, Philadelphia (1988). As an example, surgical procedures for blepharoplasty are complex. Inappropriate or poorly

5 performed surgery may result in an adverse cosmetic result, or may place the patient at risk for developing vision-threatening complications. Custer, P.L., Lower eyelid blepharoplasty, in Bosniak, S., editor, Principles and Practice of Ophthalmic Plastic and Reconstructive Surgery, pp. 617-625, 624, W.B. Saunders, Philadelphia (1996).

Lasers have been employed in cosmetic and reconstructive surgery.

10 The Nd:YAG laser has been used to make incisions in the skin for face lifts (meloplasty) and for removal of bags under the eyes by blepharoplasty. Apfelberg, D.B., YAG laser meloplasty and blepharoplasty, Aesth. Plast. Surg. **19**: 231-235 (1995). However, the Nd:YAG laser's continuous wave energy may be overly thermal and cause an excessively deep zone of penetration (about 4000 μ m). The

15 CO₂ laser has been employed in blepharoplasty using the transconjunctival approach. David, L.M. The laser approach to blepharoplasty, J. Dermatol. Surg. Oncol. **14**: 741-235 (1988). While the use of laser energy has been reported to reduce bleeding during surgery and reduce pain during healing, a large incision is still required. Morrow, D.M., and Morrow, L.B.: CO₂ laser blepharoplasty. A comparison with

20 cold-steel surgery, J. Dermatol. Surg. Oncol., **18**: 307-313 (1992). The only advantage provided by the described laser technique was less swelling after surgery.

What is needed is a method of plastic surgery using a laser that provides more desirable tissue effects and which can also be used in a minimally invasive percutaneous approach.

25 SUMMARY OF THE INVENTION

A percutaneous method for the treatment of skin and subcutaneous tissue by means of an appropriate laser device capable of emitting pulses of light energy at an appropriate wavelength of less than 2 micrometers, with relatively short pulse widths, at relatively low energy per pulse and relatively rapid pulse repetition

30 rates is provided by the present invention. Light energy characterized by such parameters is applied subcutaneously to tissues underlying the skin. The method is useful for the practice of surgery, especially plastic and cosmetic surgery as well as dermatology. The method is non-invasive or minimally invasive and well suited for

outpatient therapy. In particular, application of the laser energy directly to the tissue beneath the skin eliminates or reduces the erythema that can result when laser energy is applied to the skin from outside the body.

The method of the present invention is especially suitable for several
5 procedures used in plastic and cosmetic surgery as well as dermatology. Procedures for which the method of the present invention can be used include, inter alia, the removal of pigmentation, such as lentigines (age spots), hyperpigmentation, lentigo (freckles), café-au-lait macules, actinic keratosis, melasma, and tattoos (body or facial). The method of the present invention can also be used for the removal of
10 plantar warts, chin reshaping via the percutaneous laser melting or desiccation of fat, amelioration of turkey neck, and the treatment of some dilated blood vessels associated with rosacea. The method of the present invention is also suitable for coagulation of spider veins (< 1 mm), removal of keloid scars, coagulation of varicose veins (> 1 mm), reshaping of the upper lip, reshaping of the eyelids,
15 permanent ablation of the hair follicle to permanently prevent hair regrowth and some types of otoplasty. The method of the present invention is also suitably used for the treatment of various cutaneous vascular lesions, such as port wine stains, hemangiomas, and telangiectasias, including those of the face and the leg.

The method of the present invention can also be used for plastic
20 surgery treatments such as skin resurfacing, removal of perioral, periorbital and ear lobe wrinkles, treatment of nasal labial folds, perioral fat pads and marionette lines, lip lift, neck lift, eyebrow lift, lipolysis (of upper and lower eyelids, cheeks, abdomen, thighs), blepharoplasty, rhinoplasty, hair transplantation, treatment of polly beak and internal weir (nostril reduction). Scars that can be treated using the method
25 of the present invention include acne scars, keloids, chicken pox scars, stretch marks (striae), hypertrophic scars, and skin graft hypertrophy as well as pits and depressions. In addition, the method of the present invention is also suitable for burn debridement, and for the treatment of corns, papilloma (warts, condylomas, polyps) and skin cancer, including basal cell carcinoma.

30 A conventional pulsed or continuous wave laser having a wavelength of less than 2 micrometers can be converted, in accordance with the present invention, to produce pulses of variable pulse-width at various energy levels. Suitable lasers include, for example, excimer lasers, argon lasers, KTP lasers, 1.064

μm Nd:YAG lasers, 1.44 μm Nd:YAG lasers, 1.34 μm Nd:YAP lasers, 1.33 μm Nd:SFAP lasers, cobalt-magnesium-fluoride lasers, diode lasers and erbium (1.55 μm erbium:YAG, 1.73 μm erbium:YLF, 1.535 μm Er:Yb fiber and erbium:YSSG) lasers. Different depths of penetration of laser energy in tissue are achievable with
5 these and other lasers. Consequently, different rates of vaporization, different types of tissue effects and different depths of coagulation or collagen shrinkage can be obtained. Alternatively, a source of intense white light such as that obtained from a high intensity white light generator can be used.

Energy from a relatively low power, short pulse-width, high
10 repetition rate laser, applied percutaneously through an optical fiber or hollow waveguide, can avoid burning or charring the skin, or the tissue beneath the skin, while accomplishing the desired beneficial physiologic effect. At lower energy densities, the collagen component of tissue can be cross linked, reducing its volume and causing shrinkage of the tissue. Additionally, the method of the present
15 invention allows for the melting or desiccation of subcutaneous fat by the use of a relatively small diameter optical fiber, e.g. a 25-400 μm core diameter, that is introduced through the skin. The small diameter of the optical fiber, coupled with the low energy used, typically about 3 to 100 millijoules per pulse (mJ/pulse), the narrow pulse-width, typically less than 200 microseconds (μs), and relatively fast
20 repetition rate, generally 20 to 80 pulses per second (Hz), allow the fiber to penetrate the skin and be used subcutaneously upon tissue without perceptible charring as a result. Preferably, an energy level of about 3 mJ/pulse to about 20 mJ/pulse is used while the tip of the optical fiber is inserted through the skin.

A laser containing two or more laser energy producing cavities
25 (resonators) may employ a mechanism for either producing a rapid train of single, evenly spaced pulses up to 80 Hz, or emitting one pulse alongside another (double pulse) with a pulse width of up to 700 μs at a frequency up to 40 Hz, for greater coagulative effect or for vaporizing relatively harder tissues, such as bone.

The laser source typically comprises a housing containing the laser
30 generating unit as well as optical and electronic control components therefor. The optical fiber is connected proximally to the light output of the laser and extends distally through a hand piece held by the surgeon. The light energy produced by the laser source is introduced into the proximal end portion of the optical fiber, which

itself passes through a handpiece, and is emitted from the bare distal tip of the optical fiber distally to the target tissue. The tip of the optical fiber preferably has a core diameter of about 25 μm to 400 μm , more preferably about 50 μm to about 200 μm .

The face of the optical fiber tip is preferably aligned at a right angle to its longitudinal axis. Alternatively, the face of the optical fiber tip can be aligned at an angle of less than 90 degrees to its longitudinal axis, producing a beveled end that facilitates fiber entry through the skin. In other embodiments, the tip of the optical fiber is conical or wedge-shaped. Once inside tissue, endogenous fluids, or injected fluids, such as saline or local anesthetic, cause the fiber to emit laser energy in a manner similar to an optical fiber that has an end face aligned at a right angle to its longitudinal axis.

In order to obviate or at least minimize thermal damage, scarring and pigmentation changes of the skin at the entry point of the optical fiber, the fiber preferably is passed through the skin without lasing through an existing opening in the skin provided by a trocar puncture or through the entry site of a hypodermic needle used to inject saline and/or anesthetic.

Lasing can be commenced after the fiber is at least about 2-3 mm into the tissue. Lasing is stopped on fiber withdrawal when the distal end of the fiber is about 2-3 mm from the entry point.

Alternatively, bleeding at the entry and exit point can be minimized by lasing at extremely low energy, as low as 1 mJ/pulse with a very short pulse width, preferably 10-30 μs , during insertion or withdrawal of the optical fiber through the skin.

In another embodiment, the bare distal tip of the optical fiber is encased or slidably disposed within a hypodermic needle which is inserted through the skin at about a ninety-degree angle (normal to the surface). Once through the skin, the hypodermic needle and optical fiber together are aligned to a course substantially parallel to the skin and to or through underlying tissue. The hypodermic needle and optical fiber together, or the optical fiber alone, are advanced through the tissue.

The method aspect of the present invention includes a subcutaneous advancement phase as well as a withdrawal phase. In use, after penetration of the skin as described above, the tip of the optical fiber is moved forwardly through the

tissue during the advancement phase. During this phase, the tip of the optical fiber is advanced through the tissue for the desired distance without emission of laser energy or with laser emission at a controlled power level chosen to achieve the effect desired. If desired, laser energy can be emitted from the tip during advancement at a controlled energy level of less than about 3 to about 20 mJ/pulse, at a frequency of 20 to 80 Hz and a pulse width of 30 to 100 μ S. A preferred energy emission frequency during the advancement phase is about 50 to 60 Hz. During advancement, very low emission energy of 3-10 mJ/pulse can be used to facilitate the advancement of the optical fiber and prevent tissue adherence to the optical fiber. If desired, laser energy to obtain a desired therapeutic effect can be emitted at an energy of 5 to 50 mJ/pulse.

The tip of the optical fiber may be maintained at the position of furthest advance and laser energy emitted there, or alternatively, the tip may be immediately withdrawn. During the period while the tip of the laser probe is being used to treat the tissue at a selected site, laser energy can be emitted at an energy of about 5 to about 50 mJ per pulse at a frequency of about 20 to about 60 Hz. During the withdrawal phase, laser energy can be emitted at about 5 to about 50 mJ/pulse at a frequency of about 20 to about 60 Hz, depending on the tissue effect desired, or at about 3 to about 10 mJ/pulse to prevent tissue adhering to the fiber during withdrawal. In other cases, the fiber can be withdrawn without using laser energy. The energy level can also be changed as the fiber moves from one area to another under the skin to obtain a desired effect. It is not necessary to remove the optical fiber, or to turn off the laser while the surgery is being performed.

In general, the level of light energy emitted during the withdrawal phase is equal to or greater than the emission level, if any, during the advancement phase. The power output, frequency and pulse-width can be varied as required to achieve the desired result, based on the surgeon's clinical experience.

DETAILED DESCRIPTION OF THE INVENTION

The method of the present invention initially produces a subcutaneous tunnel or cavity through the tissue as the tip of the optical fiber is moved forwardly during the advancement stage, or rearwardly during the withdrawal stage, usually while emitting light energy at a relatively low energy level and a relatively short pulse width. However, in some cases, for example, if extremely thin

skin could be damaged by emitting light energy during advancement or withdrawal, the tip of the optical fiber can be advanced or withdrawn without emitting light energy. Likewise, the tip of the optical fiber can be advanced via a hypodermic needle or a cannula through friable tissue without emitting light energy.

5 The selected area is treated by repeated advancement and withdrawal cycles of the tip of the optical fiber as appropriate. These cycles may be performed in one or more directions through the same opening made by the insertion of the fiber or by the hypodermic needle containing the fiber. Each cycle may be directed at the same or a different radial angle. However, to avoid damage to blood
10 vessels which may be situated substantially normal to the skin's surface, the optical fiber is moved unidirectionally rather than so as to sweep laterally through a sector like a windshield wiper. Advancement and withdrawal cycles are repeated as appropriate through other openings within the selected region, until the entire region has been treated. The position of the tip of the optical fiber during treatment is
15 controlled in three dimensions either manually or by computer controlled positioning means, e.g., those used for positioning robotically controlled tools, if desired.

 Tissue can be removed or affected by several processes, including vaporization; cross linkage, which produces shrinkage; disruption of cellular
20 membranes; desiccation of fat cells; lipolysis or melting of fat cells; melting and fusion of tissue components (welding) and denaturation or coagulation of proteins. Little bleeding occurs during such processes due to the hemostasis produced by the effects of the applied light energy. The effects produced depend on the wavelength and energy level used. The process of tissue ablation requires relatively higher energy levels. Tissue welding may be used to join opposed tissue surfaces at
25 relatively low energy levels, without the need for sutures and their subsequent removal.

 Blood and tissue coagulation is produced by heating the tissue to at least about 62 degrees Celsius. Tissue vaporization or ablation is produced by heating the tissue to at least about 100 degrees Celsius, causing the water in the cells
30 to turn into steam. The small volume of steam produced is rapidly cooled by interaction with the tissue, and quickly condenses. Tissue disruption may also be caused by attendant concurrent acoustic effects of laser energy emission.

The physiological response of the treated area progresses through a continuum of at least three phases of wound healing after superficial or percutaneous laser treatment. First, there is an edema phase, seen many cases within about 10 days after treatment. The sequence of events generally follows a course including
5 two days of swelling and two days of subsidence. The second phase is characterized by the proliferation of fibroblasts. The third phase is the resolution phase in which tissue remodeling takes place.

The tissue in the region to be treated subcutaneously is preferably hydrated before laser treatment by the injection of water or an aqueous saline
10 solution. The water or aqueous saline solution used for this purpose may include an acceptable local anesthetic. The overall treatment parameters of energy levels, pulse width and frequency typically used in illustrative procedures are tabulated in Table 1, below.

In each case, for penetration of the skin, the optical fiber is
15 positioned perpendicular to the skin, and a very low level of light energy is emitted while very gentle pressure is applied. Typical parameters used for skin penetration are 3-10 mJ/pulse, preferably about 5 mJ/pulse, frequency of about 20-60 Hz and pulse width of about 40-80 μ S, although skin penetration of the fiber optic can be achieved also through a trocar, hypodermic needle or an opening in the skin such as a
20 needle puncture.

Similar energy parameters can be used to prevent or minimize tissue adherence while advancing the fiber to the treatment site or withdrawing the fiber from the treatment site. The preferred energy parameters for treatment at the site or along a tissue track, are set forth in Table 1.

TABLE 1
Preferred Parameters for Laser Treatment
in Selected Procedures

	PROCEDURE	FREQUENCY Hz	ENERGY mJ/Pulse	PULSE WIDTH (μ S)
5	Upper Blepharoplasty	20-60	5-40	50-80
	Lower Blepharoplasty	20-60	5-40	40-70
	Varicose Vein Coagulation	20-60	5-40	70-90
	Varicose Vein Coagulation, Double pulse Mode*	10-50	10-100	600-700
10	Skin Wrinkle Removal	20-60	5-40	40-70
	Telangiectasia	20-60	5-40	40-100
	Permanent Hair Removal	20-60	5-20	40-70

* Double pulse mode can be used to achieve long pulse width for greater coagulative effect
 (see EXAMPLE 8, below).

The laser tissue effect on the selected tissue site can be controlled by modulating the energy per pulse, repetition rate and/or pulse width of the emitted laser energy.

EXAMPLE 1

SUBCUTANEOUS LOCALIZED

TREATMENT PARALLEL TO THE SKIN SURFACE

The areas selected for treatment are first hydrated by an injection of water, an aqueous saline solution, or, preferably, an aqueous saline solution containing an appropriate local anesthetic. The injected liquid serves to absorb excess light energy and heat, to cool the tissue and to provide a buffer zone, which is especially useful in some locations, such as around the eyes.

The tip of the optical fiber is placed on the skin surface, at about a 90 degree angle to the skin surface. The optical fiber is a bare optical fiber of about 100 μ m to about 365 μ m in core diameter, preferably about 200 μ m core diameter. The tip pierces the skin and is advanced into the subcutaneous tissue while emitting laser energy at about 5 mJ/pulse, a pulse width of about 40 to about 70 μ S at a

frequency of about 20 to about 60 Hz. Low energies are used to minimize adverse thermal effects, such as scarring, depigmentation or hyperpigmentation, at the site of entry.

After insertion of the tip of the optical fiber through the skin, the fiber is turned so that it is roughly parallel to the plane of the skin surface. The fiber is advanced and withdrawn repeatedly as needed to treat the selected region. Energy emission at 1.55 μm is increased after the initial advancement stage to a therapeutic level of about 5 to about 50 mJ/pulse, depending on the diameter of the fiber, smaller fibers requiring less energy. Preferably, about 20 mJ/pulse is used at about the same pulse width and frequency. The optical fiber is moved axially to and from, but not swept laterally like a windshield wiper. The treatment of a selected area is continued until audible cavitation sounds ("popping") cease. Such cavitation sounds signal the destruction of the fat present at the site (lipolysis) and the heating of the collagen. The optical fiber is then withdrawn from the skin, while continuing to emit energy at or below the therapeutic level, in order to minimize the amount of tissue adhering to the tip of the optical fiber.

This method is used when the primary objective is the removal of fat or the coagulation of blood vessels, with a secondary objective of tightening the skin. This method is appropriate, for example, for lipolysis of the fat pads and tightening (blepharoplasty) of the upper and lower eyelids, removal of nasal labial folds, removal of perioral and periorbital wrinkles; treatment of marionette lines and wrinkles of the ear lobes; neck lifts and lip lifts. This method can also be used for coagulation of telangiectasias, varicose and spider veins, hemangiomas and rosacea.

EXAMPLE 2

PERCUTANEOUS LOCALIZED

TREATMENT NON-PARALLEL TO SKIN SURFACE

The method of Example 1 is used with the modification that the optical fiber is directed to the treatment site or used along a treatment track that is not parallel to the plane of the skin surface. This method is appropriate, for example, for the treatment of polly beak, wherein the shape of the nose is lifted and reshaped as desired by producing tissue shrinkage combined with lipolysis. For this purpose, the frequency used is about 20 to about 60 Hz; all other parameters as the

same as described in Example 1. This method is useful when the primary objective is the removal of fat or removal of excess vascularization, with a secondary objective of tissue shrinkage to tighten the skin.

5

EXAMPLE 3

TATTOO REMOVAL

Tattoo removal is accomplished by inserting the tip of the optical fiber through the skin in the pigmented area, at the fiber penetration energy parameters as described above, keeping the optical fiber perpendicular to the skin or
10 tilting it at an angle substantially parallel to the skin and advancing and withdrawing the optical fiber while emitting energy at the parameters as described in Example 1. Subsequent additional penetrations are made until the entire pigmented area is treated.

EXAMPLE 4

15

INCISION (INTERNAL WEIR)

A bare optical fiber about 365 μm in diameter is inserted at the base of the nostril. The method of Example 1 is used to create a wedge-shaped trough or channel; the parameters are: about 10 mJ/pulse to about 50 mJ/pulse, pulse width 50-
20 70 μs and frequency about 20 to about 60 Hz. The edges of the channel are sutured together to reduce the size of the nostril opening.

EXAMPLE 5

CARTILAGE VAPORIZATION, BONE REDUCTION

This method is useful for rhinoplasty (commonly referred to as a
25 nose job), which can be performed without postoperative bruising and black eyes. Series of holes are made through the skin and through cartilaginous and bony tissue using the optical fiber. The holes are placed at or around the nose ridge protrusion in a configuration like the perforations at the edges of a postage stamp. During the entry phase, the tip of the 200 or 365 μm bare optical fiber is placed at a 90 degree
30 angle relative to the skin. The fiber enters the skin through a trocar or needle puncture, or low penetration energies (about 5 mJ/pulse), can be used to minimize thermal effect at the skin entrance point. Therapy is administered by advancing the fiber internally through cartilaginous and/or bony tissue. Energy parameters for

therapy are 15-40 mJ/pulse, 40-70 μ S pulse width, at 20-60 Hz. After the "postage stamp" configuration is completed, external pressure is applied to the "postage stamp" to dislocate it from its original structural connections. The cartilaginous/bone fragment may be left in the body to be naturally absorbed over time.

5

EXAMPLE 6

TISSUE TRANSPLANTATION

This method is useful for removal of patches of skin bearing hairs for transplantation into bald areas where hairless skin has been removed, as well as
10 for transplantation of patches of normal skin onto burned surfaces. In both cases, the laser enables the patches to be removed without bleeding. The patches can be affixed by welding their edges to the existing tissue, with less bleeding and scabbing, and with faster healing.

The tissue is hydrated by the injection of water, saline or
15 preferably, an aqueous solution of local anesthetic, as described in Example 1. The bare patch of skin is excised using a 200-365 μ m bare optical fiber emitting energy at 20-40 mJ/pulse, 40-70 μ S pulse width, at 20-60 Hz. The patch of skin bearing hair is implanted in place, and the edges sealed to the adjacent skin using the parameters of 10-25 mJ/pulse, 30-70 μ S pulse width, 20-60 Hz.

20

EXAMPLE 7

COAGULATION OF VARICOSE VEINS

This method is useful for treatment of varicose veins. The area surrounding the veins to be treated is anesthetized. The optical fiber, preferably a
25 bare optical fiber, about 200 μ m to about 365 μ m in diameter, is placed on the skin above one end of the visible portion of the vein to be treated. The optical fiber penetrates the surface of skin at about a 90 degree angle and enters the vein, using parameters of about 5 mJ/pulse, 50-90 μ S pulse width and 20-60 Hz. The energy is increased to about 5-25 mJ/pulse, preferably about 15 mJ/pulse, with the optical fiber
30 tip within the vein. Treatment is continued until the vein is coagulated. After the treatment, the tip of the optical fiber is withdrawn while lasing at the therapeutic parameters, i.e. about 5-25 mJ/pulse, preferably about 15 mJ/pulse, 70-90 μ S pulse

width and 20-60 Hz. The treatment is repeated at the other end of the visible portion of the varicose vein.

Alternatively, a laser generating energy in a double pulse mode is used in the treatment of varicose veins. In the double pulse mode, a periodic burst of pulses comprising two or more pulses close together in time is produced (instead of a train of equally spaced pulses), thereby increasing the effective duration of the pulse length and thus the coagulative effect. The treatment protocol as described above is modified by the use of pulses about 600 μ S to about 700 μ S in width at about 10 Hz to about 30 Hz. The energy levels used are the same as described above, i.e. about 5 mJ/pulse during penetration and about 15 mJ/pulse during therapy. In relatively larger veins, up to 50 mJ per pulse is emitted to coagulate a relatively larger volume of blood.

EXAMPLE 8

PERMANENT HAIR REMOVAL

Hair removal is accomplished by inserting a small diameter optical fiber directly into the hair follicle, and applying an appropriate amount of laser energy, i.e., sufficient to coagulate or vaporize the hair follicle. This treatment disables the follicle and prevents regrowth of the hair. The diameter of the tip of the optical fiber is in the range of about 25 μ m to about 100 μ m. Preferably the diameter of the tip of the optical fiber is about 50 μ m. While the fiber may be manually inserted into the hair follicle, with the user employing a loupe or a magnifying device, for the treatment of large areas, a computer-controlled three dimension, x, y, z axis positioning device, as is used in industry for robotically applied tools, along with an optical scanner programmed to recognize hair follicles may be used. Laser energy parameters that are useful are: 5-25 mJ/pulse, 30-70 μ S pulse width, 20-60 Hz.

The foregoing is intended to be illustrative of the present invention, but not limiting. Numerous variations and modifications may be effected without departing from the true spirit and scope of the invention.

CLAIMS:

1. A method for percutaneous laser treatment of a patient having a condition requiring treatment, comprising the steps of:
 - selecting the area to be treated;
 - 5 selecting an appropriate source of light energy having a wavelength of less than 2 micrometers;
 - selecting an optical fiber of appropriate core diameter;
 - inserting the tip of the optical fiber through an opening in the patient's skin into tissue;
 - 10 advancing the tip of the optical fiber through tissue;
 - treating the tissue;
 - withdrawing the tip of the optical fiber through the tissue; and
 - emitting the light energy through the tip of the optical fiber at an energy level less than about 200 milliJoules per pulse, with a pulse width less than
 - 15 about 200 microseconds and at an energy emission frequency of greater than about 5 Hertz while treating the tissue.
2. The method of claim 1 wherein the light energy is laser energy and further comprising the step of emitting pulsed laser energy through the tip of the optical fiber at an energy level less than about 200 milliJoules per pulse, with
- 20 a pulse width less than about 200 microseconds and at an energy emission frequency of greater than about 5 Hertz while advancing the tip of the optical fiber.
3. The method of claim 1 wherein the light energy is laser energy and further comprising the step of emitting pulsed laser energy through the tip of the optical fiber at an energy level less than about 200 milliJoules per pulse, with
- 25 a pulse width less than about 200 microseconds and at an energy emission frequency of greater than about 5 Hertz while withdrawing the tip of the optical fiber.
4. The method of claim 2 wherein light energy is emitted through the tip of the optical fiber at a selected energy level less than about 100 milliJoules per pulse, with a pulse width less than 100 microseconds and at an
- 30 energy emission frequency greater than about 20 Hertz while the tip of the optical fiber is advanced through the tissue.
5. The method of claim 1 further comprising the step of emitting light energy from the tip of the optical fiber while the tip of the optical fiber

is inserted through the skin at an energy level of about 3 milliJoules per pulse to about 20 milliJoules per pulse.

6. The method of claim 2 wherein the energy emission level while the tip of the optical fiber is advanced through the tissue is about 3 milliJoules per pulse to about 20 milliJoules per pulse.

7. The method of claim 2 wherein the energy emission frequency while the tip of the optical fiber is advanced through tissue is about 20 to 80 Hertz.

8. The method of claim 5 wherein the energy emission frequency while the tip of the optical fiber is inserted through the skin is about 20 to 80 Hertz.

9. The method of claim 2 wherein the energy emission level while the tip of the optical fiber is advanced through tissue is about 5 milliJoules per pulse to about 50 milliJoules per pulse.

10. The method of claim 3 wherein the energy emission level while the tip of the optical fiber is withdrawn through tissue is about 5 milliJoules per pulse to about 50 milliJoules per pulse.

11. The method of claim 2 wherein the energy emission frequency while the tip of the optical fiber is advanced through tissue is about 20 to about 80 Hertz.

12. The method of claim 3 wherein the energy emission frequency while the tip of the optical fiber is withdrawn through tissue is about 20 to about 80 Hertz.

13. The method of claim 1 wherein the pulse width is 5 to 100 microseconds.

14. The method of claim 1 wherein the light energy is obtained from a Nd:YAG laser.

15. The method of claim 1 wherein the light energy is obtained from an excimer laser.

16. The method of claim 1 wherein the light energy is obtained from an argon laser.

17. The method of claim 1 wherein the light energy is obtained from a KTP laser.

18. The method of claim 1 wherein the light energy is obtained from a diode laser.
19. The method of claim 1 wherein the light energy is obtained from a 1.064 μm Nd:YAG laser.
- 5 20. The method of claim 1 wherein the light energy is obtained from a erbium laser.
21. The method of claim 1 wherein the light energy is obtained from a high intensity white light generator.
22. The method of claim 1 wherein the tissue is skin tissue.
- 10 23. The method of claim 1 wherein the tissue is tissue underlying the skin.
24. The method of claim 1 wherein the condition requiring treatment is blepharochalasis.
25. The method of claim 1 wherein the condition requiring
15 treatment is dermochalasis.
26. The method of claim 1 wherein the condition requiring treatment is turkey neck.
27. The method of claim 1 wherein the condition requiring treatment is rosacea.
- 20 28. The method of claim 1 wherein the condition requiring treatment is plantar warts.
29. The method of claim 1 wherein the condition requiring treatment is keloid scars.
30. The method of claim 1 wherein the condition requiring
25 treatment is telangiectasia.
31. The method of claim 1 wherein the condition requiring treatment is wrinkles.
32. The method of claim 1 wherein the condition to be treated is unwanted hair follicles.
- 30 33. The method of claim 1 wherein the condition to be treated is the pigmented area of a tattoo.
34. The method of claim 1 wherein the condition requiring treatment is marionette lines.

35. The method of claim 1 wherein the condition requiring treatment is basal cell carcinoma.

36. The method of claim 1 wherein the condition requiring treatment is acne scars.

5 37. The method of claim 1 wherein the condition requiring treatment is chicken pox scars.

38. The method of claim 1 wherein the condition requiring treatment is age spots.

10 39. The method of claim 1 wherein the condition requiring treatment is hemangioma.

40. The method of claim 1 wherein the condition requiring treatment is port wine stains.

41. The method of claim 1 wherein the condition requiring treatment is hyperpigmentation.

15 42. The method of claim 1 wherein the condition requiring treatment is varicose veins.

43. The method of claim 1 wherein the condition requiring treatment is polly beak.

20 44. The method of claim 1 wherein a laser emitting energy in a double pulse mode is used to produce an effective pulse width of up to about 700 μ S and wherein the condition requiring treatment is varicose veins.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/21040

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61B 17/36

US CL :606/03, 09, 13-16

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 606/03, 09, 13-16

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
NONEElectronic data base consulted during the international search (name of data base and, where practicable, search terms used)
NONE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5,360,425 A (CHO) 01 November 1994, entire document.	1, 2, 9, 13
Y,P	US 5,749,868 A (FURUMOTO) May 12, 1998, entire document.	1, 14-43
Y	US 5,389,096 A (AITA et al) 14 February 1995, entire document.	1-3, 7, 11, 12
Y	US 4,862,886 A (CLARKE et al) 05 September 1989, entire document.	1, 2, 3, 7, 11, 12
Y	US 5,569,240 A (DOWLATSHAHI et al) 29 October 1996, entire document.	3, 10
Y	US 5,531,739 A (TRELLES) 02 July 1996, entire document.	1, 14-43



Further documents are listed in the continuation of Box C.



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* Special categories of cited documents:	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
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INTERNATIONAL SEARCH REPORT

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PCT/US98/21040

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4,370,642 A (COSTELLO et al) 25 January 1994, entire document.	1-43



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(21) International Application Number: PCT/US98/25412 (22) International Filing Date: 1 December 1998 (01.12.98) (30) Priority Data: 08/980,625 1 December 1997 (01.12.97) US (71) Applicant (for all designated States except US): ESC MEDICAL SYSTEMS LTD. [IL/IL]; P.O. Box 240, 20692 Yokneam (IL). (71) Applicant (for TJ only): FRIEDMAN, Mark, M. [US/IL]; 1 Alharizi, 43406 Raanana (IL). (72) Inventors; and (75) Inventors/Applicants (for US only): KREINDEL, Michael [IL/IL]; 33 Bar Rav Hai David, 35592 Haifa (IL). ECKHOUSE, Shimon [IL/IL]; 27 Rabin Ester, Denya, 34987 Haifa (IL). (74) Common Representative: FRIEDMAN, Mark, M.; c/o Castorina, Anthony, Suite 207, 2001 Jefferson Davis Highway, Arlington, VA 22202 (US).		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i>
(54) Title: IMPROVED DEPILATORY METHOD AND DEVICE (57) Abstract <p>An improved method of hair removal, and associated devices. For the removal of shallow and/or light-colored hair, the targeted skin region is irradiated with light of a wavelength between 550 nm and 680 nm, and an energy density of between 30 J/cm² and 100 J/cm², for between 1 ms and 100 ms. A targeted area about as wide as the depth of the hair follicles to be destroyed is irradiated using one or more sources, such as lasers, that produce considerably narrower beams, either by scanning one beam across the target or by irradiating the target using several beams simultaneously.</p>		

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APPLICATION FOR PATENT

5

Title: IMPROVED DEPILATORY METHOD AND DEVICE

10 FIELD AND BACKGROUND OF THE INVENTION

The present invention relates to hair removal and, more particularly, to an improved method and device for permanently removing hair using pulses of light.

The use of intense light to heat hairs, and the follicles whence they grow, to temperatures high enough to kill the follicles without appreciable damage to the surrounding
15 tissue, is known. Tankovich, in US Patent No. 5,226,907, teaches a method of hair removal in which the portion of the hair below skin level is coated with a substance such as carbon that absorbs light of selected frequencies (10.6 micron infrared light in the preferred embodiment) than the surrounding tissue. Anderson et al., in US Patent No. 5,595,568, which is incorporated by reference for all purposes as if fully set forth herein, relies on the
20 natural pigmentation of the hair to absorb light in a range of 680 nm to 1200 nm.

With the object of destroying many follicles at once, both Tankovich and Anderson et al. direct a light beam at least on the order of 1 cm wide at each area of skin to be treated. As noted by Anderson et al., the width of the light beam preferably is at least as great as the depth of the follicles to be destroyed. Depending on their specific location, follicles may be
25 between 0.1 mm and 0.5 mm deep. The energy density of the light beam taught by Anderson et al. is between 10 J/cm² and 200 J/cm², most preferably between 30 J/cm² and 50 J/cm². Although lasers are readily available that produce beams of coherent light with this width and energy density, it would be advantageous to be able to use less expensive diode lasers, with beam widths as small as 0.05 mm, for this application.

Figure 1 is a plot of the penetration depth of light in skin tissue, as a function of wavelength. Light in the wavelength range taught by Anderson et al., 680 nm to 1200 nm, penetrates skin tissue to depths of 2 mm or greater. Thus, a larger volume of skin tissue is heated than is strictly necessary when destroying follicles shallower than 2 mm, and there is a risk of overheating the surrounding skin tissue.

SUMMARY OF THE INVENTION

According to the present invention there is provided an improved method for removing hairs from a skin region of a patient, including the step of irradiating the skin region with light of a first wavelength shorter than about 680 nm.

According to the present invention there is provided an improved method for removing multiple hairs from a skin region of a patient, each of the hairs being in a corresponding follicle at a certain depth in the skin region, including the step of irradiating a plurality of spots in a portion of the skin region having a lateral extent at least as great as the depth of the follicles, so as to deposit at least about 30 J/cm² of energy in the portion of the skin region within a time shorter than about 200 ms.

According to the present invention there is provided a device for sequentially irradiating a plurality of substantially contiguous spots in a two-dimensional pattern on a target, including: (a) a source of light; and (b) a mechanism for sequentially directing the light at each of the spots in the pattern.

According to the present invention there is provided a device for simultaneously irradiating a plurality of substantially contiguous spots in a two-dimensional pattern on a target, including: (a) an array of apertures congruent with the pattern; (b) at least one light source; and (c) a mechanism for optically coupling the at least one light source with the apertures.

Figure 2 shows experimentally measured absorption coefficients of hair of four different colors, as a function of wavelength. In the especially preferred wavelength range of Anderson et al., 800 nm - 900 nm, the absorption coefficient of dark (black, red or brown) hair is between about 50 cm^{-1} and about 70 cm^{-1} , but the absorption coefficient of blond hair is only about 25 cm^{-1} . To obtain, for blond hair, the light absorption obtained in dark hair by the method of Anderson et al., it is necessary to use light in the wavelength range of the present invention, 550 nm to 680 nm. Thus, the wavelength range of the present invention is preferred over the prior art wavelength range, both for shallow hair and for blond hair. Light in the wavelength range of the present invention may be supplemented by light in the prior art wavelength range for removing shallow dark hair. The preferred energy density and pulse length are similar to those of the prior art: an energy density between about 30 J/cm^2 and about 100 J/cm^2 , and a pulse length between about 1 ms and about 100 ms. The upper end of this time span is the maximum expected thermal relaxation time of a hair follicle enclosed in dermal fat.

In the second aspect of the present invention, the therapeutic beams of light are created by diode lasers, or similar sources, that produce collimated beams of light that are narrower than the desired depth of penetration. To achieve the desired effective beamwidth, the beam or beams are directed at multiple spots within a region of skin whose lateral extent is as great as the desired depth of penetration. One beam may be directed sequentially at several spots within the region, or several beams may be directed simultaneously at the several spots within the region, as long as the desired energy density of at least about 30 J/cm^2 is deposited within the desired time of no more than about 200 ms.

The preferred range of spot diameters within the scope of the present invention is between about 0.5 mm and about 5 mm. A spot as small as 0.5 mm in diameter may require an energy density as high as about 1000 J/cm^2 .

The scope of the present invention also includes devices for effecting this irradiation with an effective beamwidth wider than the collimated beam produced by the light source. In one embodiment of the device, a diode laser is optically coupled to a proximal end of an optical waveguide that is about as wide as the collimated beam produced by the laser, and the other, distal end of the waveguide is scanned across the target region. In another embodiment, several diode lasers are optically coupled to the proximal ends of several optical waveguides, and the distal ends of the waveguides are bundled in a two dimensional pattern that is as wide as the desired effective beamwidth. Most preferably, the distal ends of the waveguides are inserted in a spacer which, when held against the target, holds the distal ends of the waveguide stationary with respect to the target and at a fixed distance from the target.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention is herein described, by way of example only, with reference to the accompanying drawings, wherein:

FIG. 1 is a graph showing the penetration depth of light of various wavelengths in skin tissue;

FIG. 2 is a graph showing the absorption coefficient of hair of various colors as a function of wavelength;

FIG. 3 shows an irradiation pattern of the present invention superposed on a prior art irradiation pattern;

FIG. 4 is a schematic depiction, partly in perspective, of a first device of the present invention;

FIG. 5 is a schematic depiction, partly in perspective, of a second device of the present invention.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

The present invention is of a method and device which can be used to remove unwanted hair.

5 The principles and operation of depilation according to the present invention may be better understood with reference to the drawings and the accompanying description.

Referring now to the drawings, Figure 3 shows a square **10** that is 3 mm on a side. Superimposed thereon is a pattern of **16** partly overlapping circles **12**, each 1 mm in diameter, for the equivalent irradiation of a skin region according to the present invention.

10 To deposit 30 J/cm^2 of light energy in the area of square **10** within 75 msec requires a 36W laser. To deposit the same 30 J/cm^2 sequentially in circles **12** within 75 msec (4.7 msec per circle) requires a 50W laser. To deposit the same 30 J/cm^2 simultaneously in circles **12** within 75 msec requires 16 3W lasers.

Figure 4 shows, schematically, a device **20** for effecting the sequential irradiation of
15 circles **12**. The mechanical portion of device **20** is based on a rigid hollow rectangular frame **22**. Rising from three of the corners of frame **22** are three towers **24**, **26** and **28**. Tower **24** supports a stepping motor **36** which rotates a mirror **30** about a vertical rotation axis. From tower **26** projects an arm **34** which supports a second stepping motor **38**. Stepping motor **38** rotates a mirror **32** about a horizontal rotation axis. Tower **28** supports a clamp **40** which
20 secures a distal end **46** of an optical waveguide **44** to tower **28** so that distal end **46** of optical waveguide **44** points at mirror **30**. Waveguide **44** is circular in cross section and 1 mm in diameter. The combined rotations of mirror **30** in a horizontal plane and mirror **32** in a vertical plane directs light emerging from distal end **46** of optical waveguide **44** to any desired lateral position within the interior of frame **22**.

A proximal end 48 of waveguide 44 is optically coupled to a laser 50 having an output power of 50W. Laser 50 is energized and controlled by a microprocessor-based control system 52 via a power/control line 54. Stepping motors 36 and 38 are energized and controlled by control system 52 via a power/control line 56.

To use device 20, frame 22 is positioned to enclose the targeted skin region. Control system 52 then sequentially rotates mirrors 30 and 32 to direct the light emerging from distal end 46 to each of circles 12 in the pattern of Figure 3, spending 4.7 msec at each circle 12 while firing laser 50. Distal end 46 functions in combination with mirrors 30 and 32 as an optical aperture, wherefrom light from laser 50 emerges to irradiate the target. Laser 50 may be pulsed, with the pulses thereof synchronized with the rotations of mirrors 30 and 32 so that the pulses are directed at each of circles 12. Alternatively, laser 50 may operate continuously, with mirrors 30 and 32 providing a dwell time of 4.7 msec at each of circles 12.

Figure 5 is a partial schematic depiction of a device 60 for effecting the simultaneous irradiation of circles 12. 16 fiber optic waveguides 64, each of circular cross section and 1 mm in diameter, are arranged in a bundle 62 so that distal ends 66 of waveguides 64 are deployed in the pattern of circles 12 of Figure 3. Distal ends 66 of waveguides 64 are inserted together in a proximal end 74 of a hollow rectangular sleeve 70. When a distal end 76 of sleeve 70 is placed adjacent to a targeted skin region, sleeve 70 keeps distal ends 66 of waveguides 64 at the desired distance from the target. A proximal end 68 of each waveguide 64 is optically coupled to a separate 3W diode laser 72. With sleeve 70 in place above the target, lasers 72 are fired simultaneously for 75 msec. Distal ends 66 serve as apertures, wherefrom light from lasers 72 emerges to irradiate the target.

Diode lasers suitable for implementing the various aspects of the present invention are manufactured by a variety of manufacturers, for example Applied Optonics Corporation.

While the invention has been described with respect to a limited number of embodiments, it will be appreciated that many variations, modifications and other applications of the invention may be made.

WHAT IS CLAIMED IS:

1. An improved method for removing hairs from a skin region of a patient, comprising the step of irradiating the skin region with light of a first wavelength shorter than about 680 nm.
2. The method of claim 1, wherein said first wavelengths longer than about 550 nm.
3. The method of claim 1, further comprising the step of irradiating the skin region with light of a second wavelength longer than about 680 nm.
4. The method of claim 1, wherein said light has an energy density, on said skin region, of between about 30 J/cm^2 and about 1000 J/cm^2 .
5. The method of claim 1, wherein said light is directed at the skin region in at least one pulse having a duration of between about 1 ms and about 200 ms.
6. An improved method for removing multiple hairs from a skin region of a patient, each of the hairs being in a corresponding follicle at a certain depth in the skin region, comprising the step of irradiating a plurality of spots in a portion of the skin region having a lateral extent at least as great as the depth of the follicles, so as to deposit at least about 30 J/cm^2 of energy in said portion of the skin region within a time shorter than about 200 ms.

7. The method of claim 6, wherein each of said plurality of spots has a diameter between about 0.5 mm and about 5 mm.

8. The method of claim 6, wherein said irradiating is effected using light having a wavelength between about 550 nm and about 680 nm.

9. The method of claim 6, wherein said irradiating is effected using light having a wavelength between about 680 nm and about 1000 nm.

10. The method of claim 6, wherein said irradiating of said plurality of spots is effected substantially simultaneously.

11. The method of claim 6, wherein said irradiating of said plurality of spots is effected sequentially.

12. A device for sequentially irradiating a plurality of substantially contiguous spots in a two-dimensional pattern on a target, comprising:

- (a) a source of light; and
- (b) a mechanism for sequentially directing said light at each of the spots in the pattern.

13. The device of claim 12, wherein said mechanism includes an aperture wherefrom said light emerges to strike the target.

14. The device of claim 13, wherein said mechanism includes:

- (i) an optical waveguide having a proximal end and a distal end, said proximal end being optically coupled to said source of said light, said aperture including said distal end, and
- (ii) a mechanism for scanning said distal end across said pattern.

15. A device for simultaneously irradiating a plurality of substantially contiguous spots in a two-dimensional pattern on a target, comprising:

- (a) an array of apertures congruent with said pattern;
- (b) at least one light source; and
- (c) a mechanism for optically coupling said at least one light source with said apertures.

16. The device of claim 15, wherein said mechanism includes a plurality of optical waveguides, each of said optical waveguides having a proximal end and a distal end, each of said proximal ends being optically coupled to one of said at least one light source, each of said apertures including one of said distal ends.

17. The device of claim 16, including a plurality of said at least one light source, wherein each of said optical waveguides is optically coupled to a separate one of said plurality of light sources.

18. The device of claim 15, further comprising:

- (d) a spacer for holding said apertures at fixed position relative to the target.

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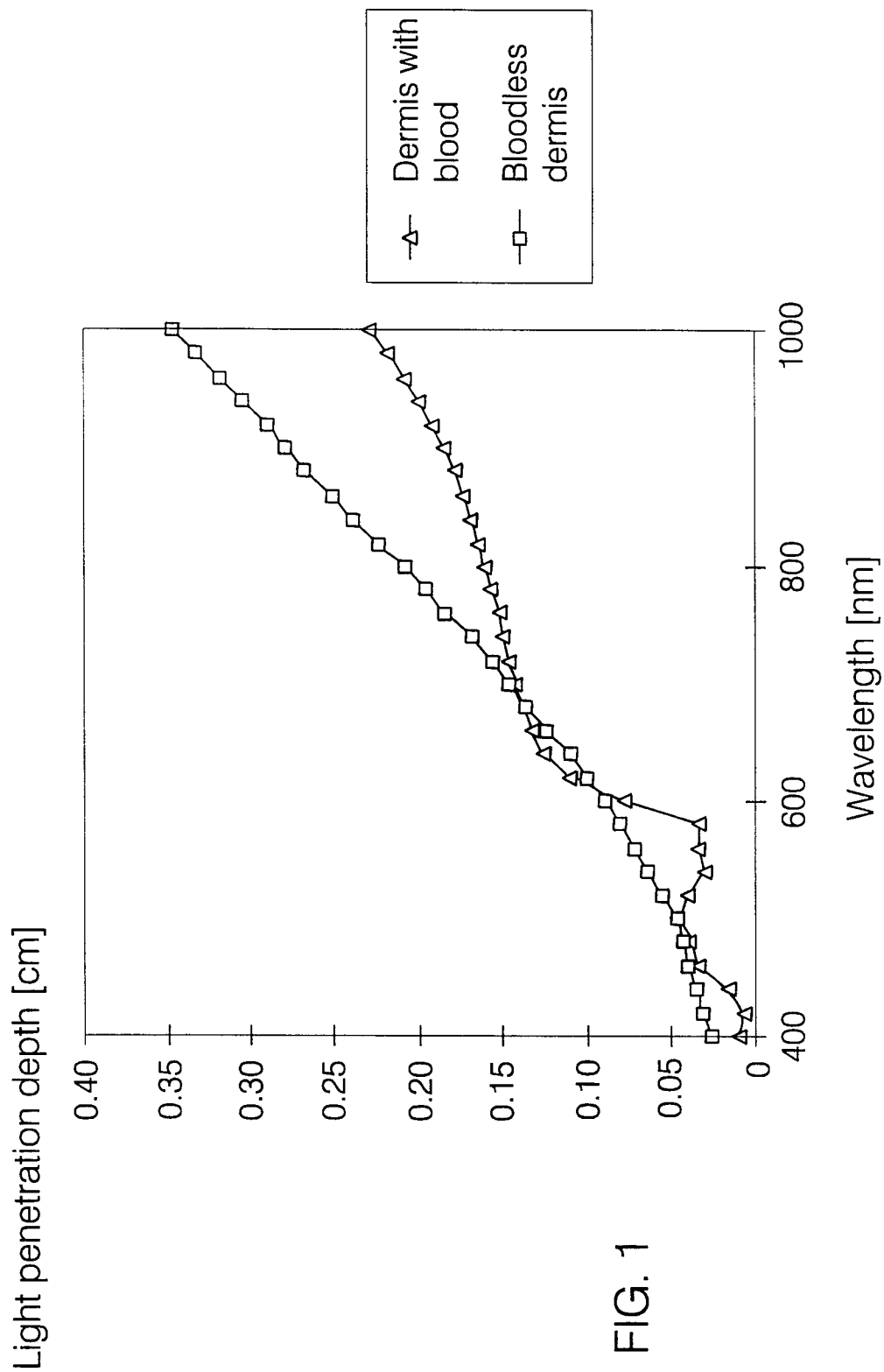


FIG. 1

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Absorption coefficient [1/cm]

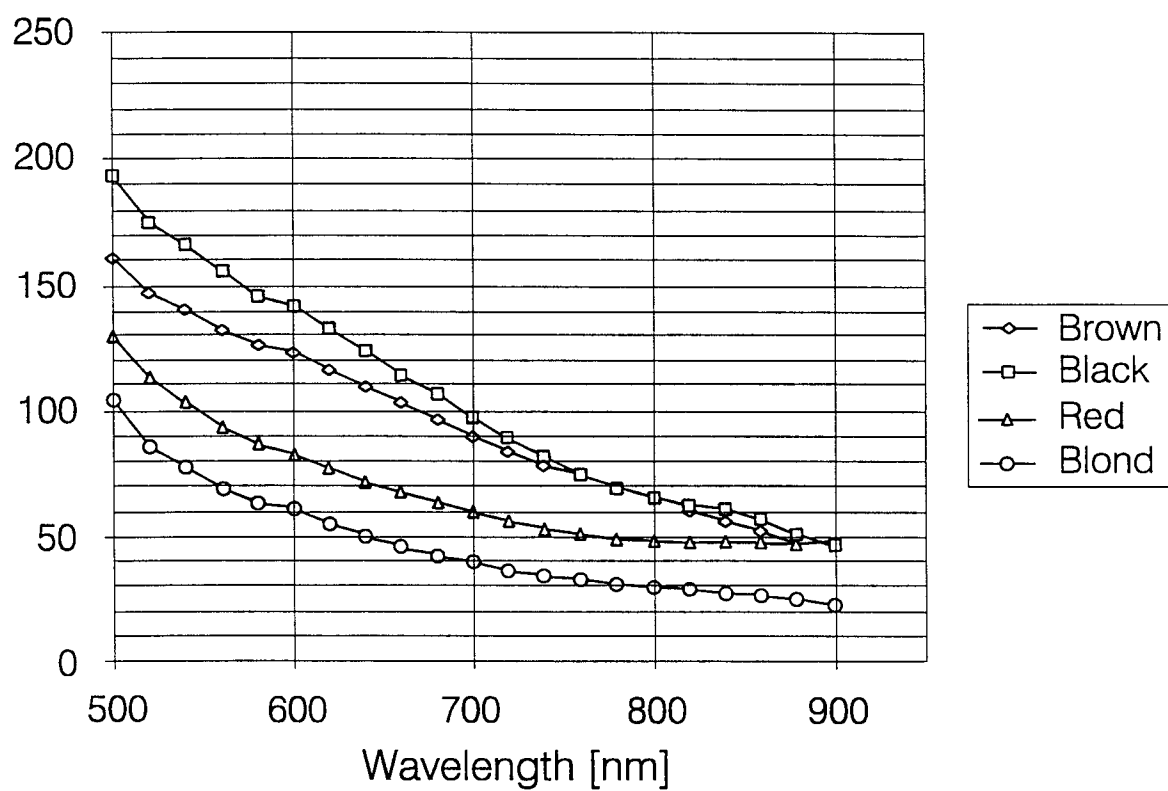


FIG. 2

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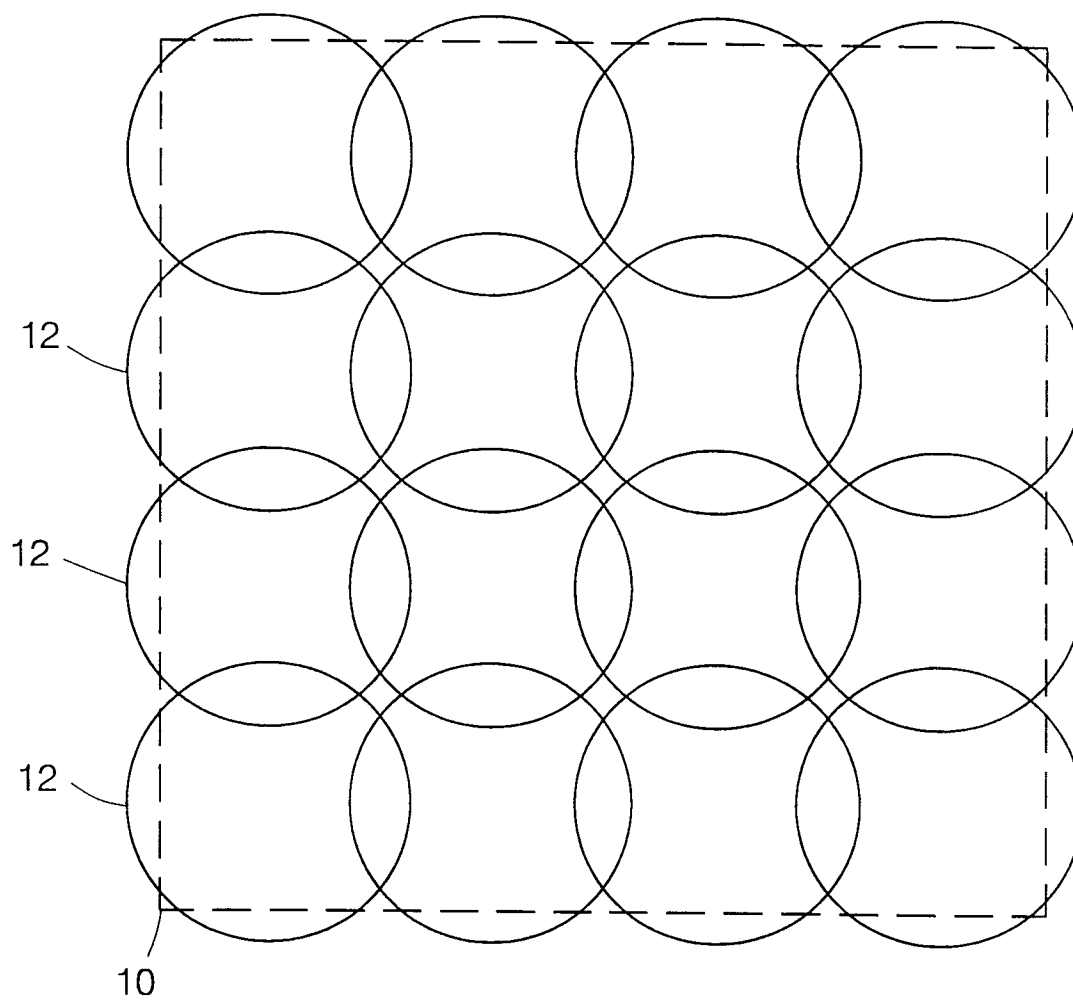


FIG. 3

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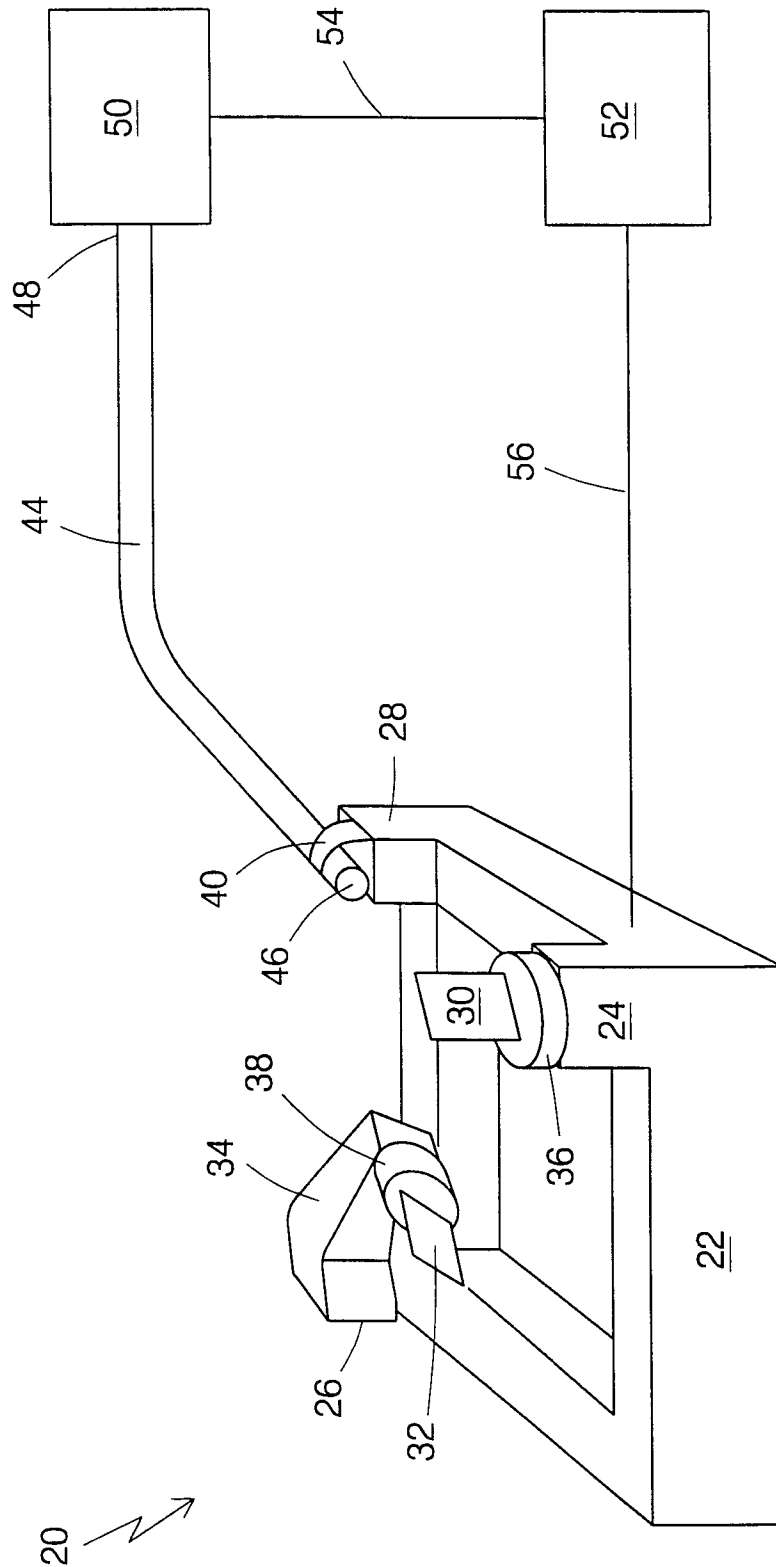
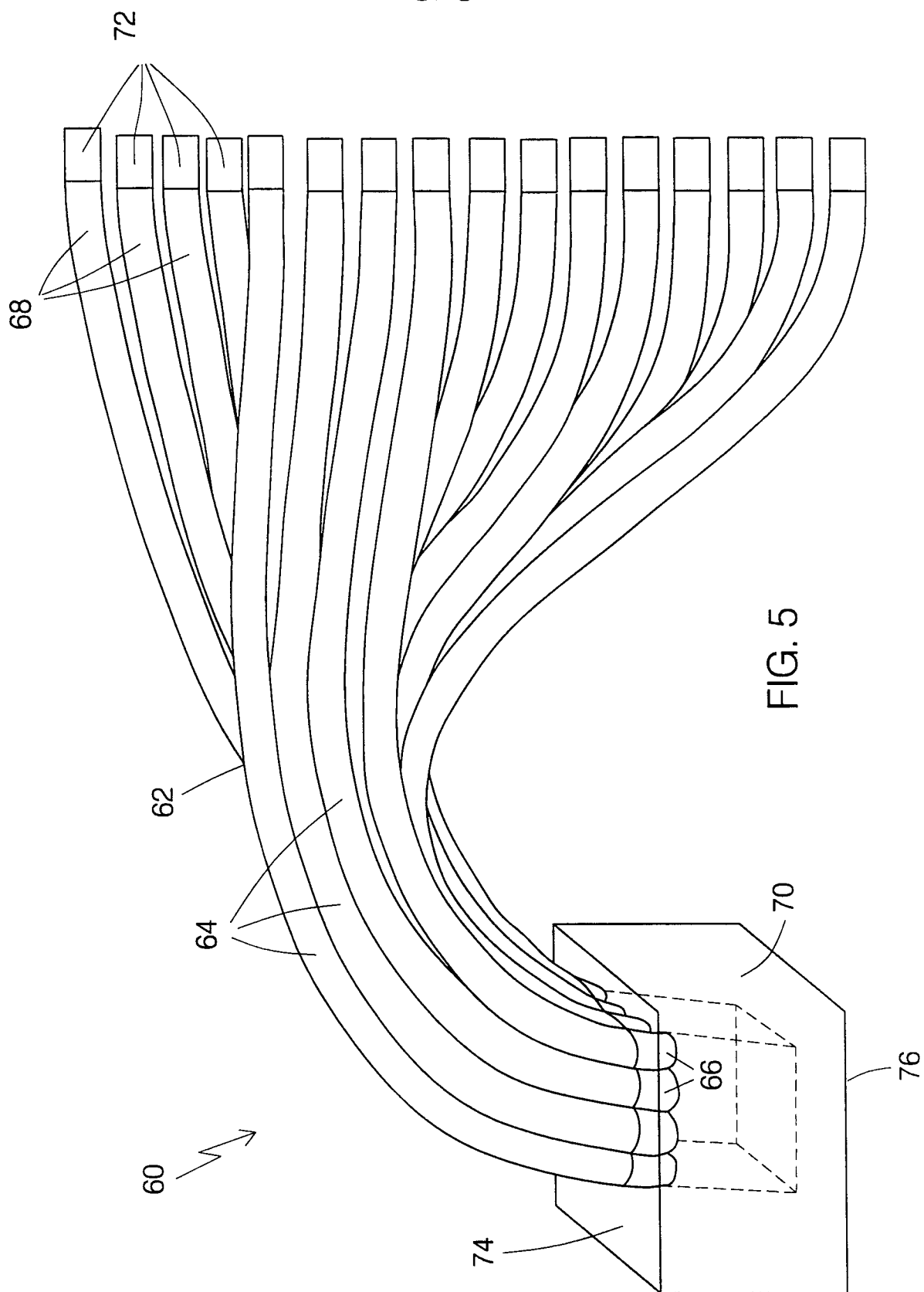


FIG. 4

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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER

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B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 606/3-18

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5,182,857 A (SIMON) 02 February 1993, entire document.	1-13
Y		14-18

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

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(21) International Application Number: PCT/US97/22347 (22) International Filing Date: 5 December 1997 (05.12.97) (71) Applicant: THERMOLASE CORPORATION [US/US]; 10455 Pacific Center Court, San Diego, CA 92121 (US). (72) Inventors: ZHAO, Zhong-Quan; 13510 Chaco Court, San Diego, CA 92129 (US). KOLINKO, Vladimir, G.; 12682 Torrey Bluffs Drive #227, San Diego, CA 92130 (US). TANKOVICH, Nikolai, J.; 9361 Stargaze Avenue, San Diego, CA 92129 (US). DASSE, Kurt, A.; 20 Kerrydale Road, Needham, MA 02192 (US). FAIRCHILD, Paul, W.; 12893 Ralston Circle, San Diego, CA 92130 (US). (74) Agents: LEARN, June, M. et al.; Fish & Richardson P.C., Suite 1400, 4225 Executive Square, La Jolla, CA 92037 (US).		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i>
(54) Title: SKIN ENHANCEMENT USING LASER LIGHT (57) Abstract <p>Methods of applying laser light to the skin, and apparatus therefor, include methods for removing hair, for bleaching hair, for transdermal drug delivery, for sensing a body function, for skin tightening, and for imaging subsurface structures are described. The hair removal methods and the hair bleaching methods include infiltrating a transparent fluid with an index of refraction greater than that of skin tissue into hair ducts to help transmit the laser light down the hair ducts. The transdermal drug delivery and body function sensing methods include exfoliating layers of the stratum corneum from a section of skin with laser light. A transdermal drug delivery patch can be placed over the exfoliated skin section, or an electrical sensor can be placed over the exfoliated skin section. The skin tightening method includes implanting a light absorbing material in the dermis of a section of skin and illuminating the skin section to disturb the dermis in such a way as to cause a healing reaction that forms more collagen fibers. The imaging system includes a confocal microscope that has been adapted to view only a time-gated portion of laser light reflected from the skin.</p>		

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SKIN ENHANCEMENT USING LASER LIGHT
CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation-in-part application of U.S. provisional application Serial No. 60/052,718, filed on July 16, 1997, and U.S. provisional
5 application Serial No. 60/033,238, filed on December 5, 1996.

This application is related to co-pending U.S. patent applications Serial No. _____, filed October 21, 1997; Serial No. 08/777,576, filed December 31, 1996; Serial No. 08/695,200, filed August 1, 1996; Serial No. 08/644,231, filed May 13, 1996; Serial No. 08/492,283, filed June 19, 1995; Serial No. 08/489,358, filed June 12, 1995;
10 Serial No. 08/489,352, filed June 12, 1995; and to U.S. application Serial No. _____, filed on even date with this application, and which is incorporated herein by reference.

TECHNICAL FIELD

The invention relates to devices and methods of applying light to the skin
15 for cosmetic hair removal, hair bleaching, tightening and strengthening the skin, imaging subsurface skin structures, transdermal drug delivery and measurement of body functions.

BACKGROUND

Unwanted body hair, particularly dark hair on the face, legs, back and
20 chest is a cosmetic concern for many people. Laser light has been used for cosmetic hair removal. To minimize damage to tissue surrounding hairs, some hair removal methods apply narrowly focused beams of light to a single hair or hair follicle. For example, U.S. Patent No. 3,834,391 to Block discloses using a probe positioned at the top of a single hair duct to direct a narrow, focused beam of light down the hair duct
25 beside the hair shaft, and thence to the papilla to coagulate papillar vessels. The Block patent also discloses that introducing mineral oil into the hair duct, for example, by rubbing it on the skin, helps transmit the light to the papilla. According to the Block patent, light energy is applied until the hair can be pulled out easily with tweezers.

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U.S. Patent No. 4,388,924, to Weissman *et al.* discloses directing a narrow, focused beam of light in short duration, high intensity pulses to the epidermis adjacent a hair such that an extension of the beam intersects a single hair follicle at an angle through the skin.

- 5 Another approach, disclosed in U.S. Patent No. 5,059,192, to Zaias, applies pulsed light having a wavelength of 694 nm, which wavelength is selected for absorption by melanosomes at the base of the hair follicle and papilla. The pulse duration is shorter than the thermal relaxation time of the melanin. The laser beam is directed from a position substantially vertically over a hair duct to the papilla.
- 10 U.S. Patent Nos. 5,226,907 and 5,425,728, to Tankovich, the entire disclosures of which are herein incorporated by reference, disclose applying a light-absorbing contaminant topically to a skin section to be treated so that a portion of the contaminant enters hair follicles. The contaminant can be a water or oil-based suspension or solution containing chromophore particles having a high absorption at or near at least
- 15 one frequency band of light. The chromophore particles, for example carbon or graphite particles, are generally sized too large to penetrate the barrier layer of the stratum corneum, but small enough to readily infiltrate the hair ducts to the hair follicles. Laser pulses are used to drive the contaminant down hair ducts and deep into hair follicles. The skin section containing the infiltrated hair follicles is then illumi-
- 20 nated with a light beam that is highly absorbed by the contaminant, but that passes readily through skin. By this procedure, the hair cells surrounding the follicle that are responsible for hair growth are damaged or destroyed by energy transferred from the irradiated contaminant to the tissue surrounding the hair follicle.

- Bleaching can make unwanted hair less noticeable. Chemical bleaching
- 25 agents typically work only on the portion of the hair shaft above the skin surface. The unbleached portion below the skin surface rises above the skin and becomes visible as the hair continues to grow. U.S. Patent No. 4,792,341, to Kozikowski *et al.*, discloses using laser light to photobleach locks of hair that have been glued to transparent plates. Kozikowski *et al.* provide a table of optimal conditions for photobleaching

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using wavelengths of 530 nm and 1.06 μm to destroy melanin in hairs that are removed from the body.

U.S. Patent No. 5,423,803, to Tankovich *et al.*, the entire disclosure of which is included by reference herein, discloses a cosmetic method of skin resurfacing using laser light to give the skin a smoother appearance. A contaminant that absorbs light is applied to the skin so as to infiltrate the contaminant in gaps and crevices between surface layers of the stratum corneum, which is composed of about 20 layers of dead cells and which helps to provide a barrier to entry of harmful substances into the skin and thence the bloodstream. The skin surface bearing the contaminant is then illuminated so that the contaminant absorbs enough energy to exfoliate the outermost three or so layers of cells in the stratum corneum without significant damage to living cells below the stratum corneum.

Confocal microscopes are capable of providing images of sections of objects in nonscattering or weakly scattering media. A sample is scanned with light at a selected focal depth. The reflected image signal is passed through a small aperture positioned in front of a photodetector. The aperture cuts off portions of the image signal scattered from outside the focal plane. However, if an object is embedded in a highly scattering media, the signal to noise ratio of the image signal becomes vanishingly small very quickly as the focal plane is moved deeper into the scattering media. Schmitt, *et al.*, in "Confocal Microscopy In Turbid Media," J. Opt. Soc. Am. A, Vol. 11, No. 8, pp. 2226-35 (Aug. 1994), report that the scattering imposes fundamental limits on the sectioning capability of the microscope. Confocal microscopes cannot image objects more than about 200-300 μm deep in tissue, such as skin.

25

SUMMARY

In one aspect, the invention provides a non-therapeutic, cosmetic method of removing hair from a section of healthy skin. Papillae that are located in hair ducts located in a section of skin include melanosomes, which absorb light. Also associated with the papillae are other naturally occurring light absorbers (chromophores), such

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as, for example, blood vessels. A fluid that is transparent to light at or near at least one frequency absorbed by at least one of the natural absorbers, *e.g.*, melanosomes, is applied to the section of skin. A portion of the fluid is caused to enter hair ducts in the section of skin. A region of the section of skin is then illuminated with pulses of light
5 at the at least one frequency. The illuminating light is directed so that a portion is conducted through the fluid to papillae in hair ducts located in the region of the section of skin. Another portion of the illuminating light is transmitted through the skin to the papillae in the hair ducts located in the region of the section of skin. At least some of the illuminating light is absorbed by a natural absorber associated with
10 the illuminated papillae, causing heating of the illuminated papillae to a temperature of about 30°-90° C above ambient skin temperature with each pulse. The method further includes inhibiting vaporizing the absorbers in the papillae, including cooling the region of the section of skin between the pulses.

In a second aspect, the invention provides a method of damaging or
15 destroying papillae at the bottom of hair ducts in a section of skin so as to inhibit the regrowth of hair from the damaged follicles. According to this method, hairs from a section of skin are first removed from their respective follicles, for example, by waxing. A contaminant that has a high absorbance of light at or near at least one frequency is then applied to the skin such that some of the contaminant enters the hair
20 ducts. The contaminant can be, for example, a mixture of carbon particles with an oil that is transparent to the at least one frequency band of light. Pulses of light from a laser at the at least one frequency are then applied to a region of the section of skin. The pulses are applied with an intensity and duration that cause at least some of the contaminant to be driven to the bottom of the hair ducts to the papillae. Additional
25 transparent oil is then applied to the section of skin to fill at least the upper portions of the hair ducts with the oil. The oil at the tops of the ducts acts as a focusing lens for further pulses of the light, and the hollow ducts filled with the clear oil then act as light pipes to transmit the light pulses to the contaminant at the bottoms of the hair shafts. These pulses are absorbed by the contaminant, and are of duration, frequency,
30 number and intensity to cause the contaminant to transfer sufficient energy to the

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papillae and tissues nourishing the papillae to damage or destroy at least some of the papillae in the region of skin illuminated by the pulses.

In another aspect, the invention provides a cosmetic method of bleaching hairs growing from a section of skin. Accordingly, this method includes applying to
5 the skin section a fluid that is transparent to light at or near at least one frequency absorbed by melanosomes, and causing a portion of the fluid to penetrate hair ducts in the skin section. The method further includes illuminating the skin section containing the hairs with light at the at least one frequency, which light is directed so that a portion of the light is conducted through the fluid in the hair ducts and absorbed by
10 melanosomes in hair shafts located in the hair ducts. The remaining portion of the light contacts the hairs above the skin surface and/or is transmitted through the skin section. Light conducted through the fluid or scattered through the skin or directly impinging on the hair shafts can be absorbed by melanosomes in the hair shafts, causing the melanosomes to explode or otherwise be destroyed so as to bleach the
15 hair shafts, including bleaching at least a portion of one or more hair shafts below the skin surface. The illumination pulse duration, frequency, and intensity are selected such that the melanosomes are destroyed but the hair remains viable.

In addition, the invention provides a method for depositing a medicinal substance into the hair ducts. According to this method, the medicinal substance is
20 encapsulated in or bound to carrier particles by conventional techniques, the carrier particles being formulated to have a slow-release property and being of a size that inhibits migration out of the ducts in between cells that line the ducts. The medicinal substance can include one or more drugs, such as a material that regulates hair growth or activity of sebaceous glands. The carrier particles can be liposomes, coacervate
25 drops, erythrocyte shadow, latex or gelatin spheres, carbon microcrystals, or the like. A suspension of the carrier particles is topically applied to a section of skin that includes hair ducts. The suspension is then caused to infiltrate into the hair ducts, for example, by rubbing, and then excess material is wiped off. This leaves a concentration of the carrier particles around the hair shaft in and around the hair duct entrances.
30 Then, the carrier substance is driven deeper into the hair ducts, for example, by

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applying mechanical or ultrasonic vibrations to the section of skin. Thus, drug delivery is localized in the hair ducts, the cells of which more readily absorb the drug or active agent than do the cells in the stratum corneum, which provides an outer covering for the skin. By employing carrier particles having different sizes, or release
5 times, drug delivery can be prolonged over a period of time. In one embodiment, the carrier particles include a material that has a high optical absorbance at or near at least one frequency band of light that penetrates skin. After the carrier particles are driven into the hair ducts, the section of skin is illuminated with pulses of laser light at the at least one frequency of sufficient intensity, duration number and frequency to cause at
10 least some of the carrier particles to release the included medicinal substance.

In still another aspect, the invention provides a method of tightening and strengthening a section of skin. According to this method, a material that has a high optical absorbance at or near at least one frequency band of light that will penetrate the skin is imbedded in the dermis. The absorbent material can be, for example,
15 carbon particles, graphite thread, or the like. A region of the section of skin is then illuminated with light at the at least one frequency band, some of which light penetrates the skin and is absorbed by the absorbent material. The absorbent material transfers energy absorbed from the light to adjacent dermal tissue. This stimulates growth of new collagen fibers in the adjacent dermal tissue to add tensile strength and
20 elasticity to the area with new collagen fiber growth.

In yet another aspect, the invention provides a method of enhancing transdermal drug delivery. The method includes applying light to a section of skin to cause removal of stratum corneum cells, and then applying a drug to the section of skin from which the stratum corneum cells have been removed. The stratum corneum
25 cells can be removed a few layers at a time until about 10 to 20 layers are removed. To remove the top few layers, a contaminant is first applied to the section of skin such that the contaminant is worked into spaces between cells in the top few layers of stratum corneum cells. The contaminant has a high absorption at or near at least one frequency band of light. Pulses of light at the at least one frequency band produced by
30 a laser are then applied to a region of the section of skin. The light pulses are of an

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intensity and duration such that the contaminant absorbs enough energy with each pulse to cause cells from the top few layers to be exfoliated without causing significant harm to the layers of skin cells underneath. A transdermal drug delivery system, such as, for example, a patch, is then applied over the exfoliated region. Removing
5 layers of the stratum corneum enables the drug in the transdermal delivery system to cross the skin barrier more easily.

In a further aspect, the invention provides a method of measuring a body function with an electrical skin sensor. The stratum corneum provides an electrically resistive barrier at the skin surface. In this method, several surface layers of the
10 stratum corneum in a region of skin are first removed by the method described above. An electrical skin sensor is then applied to the region of skin and a body function is measured with the skin sensor. Removing surface layers of the stratum corneum lowers skin resistance and enables better electrical contact between the skin and the sensor.

15 In yet another aspect, the invention provides a device and method for imaging subsurface structures in a patient's skin. A highly light scattering medium, such as skin tissue, strongly attenuates the component of incident light that carries imaging information from deeply embedded objects. The attenuation results from the impossibility of focusing light in the scattering medium, the short penetration depth of
20 incident radiation, and rapid attenuation with depth of light coming out of the medium without scattering. The device of the invention includes a confocal microscope including a source of coherent light having a wavelength in a range of about 800 to about 1000 nm, and a means of time resolving light backscattered from the skin of a patient. Time resolving the signal from the confocal microscope eliminates noise
25 attributable to light multiply scattered from regions distant from the focal point of the confocal microscope, thereby improving the signal to noise ratio of the confocal microscope signal.

In yet another aspect, this invention provides a skin treatment system and process for increasing the tension and elasticity in a section of human skin. The
30 system includes an energy absorbing material deposited in the dermis portion of the

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skin, and an illumination source spaced a predetermined distance from the skin for providing energy to be absorbed by the material. The energy absorbing material can be a graphite thread sewn into the skin, or carbon particles implanted by a tattooing technique. A useful energy absorbing material has an optical absorption of at least one
5 frequency band of light emitted from the light source. The skin section can be illuminated with at least one frequency band of light, a significant portion of which penetrates the section of skin and is absorbed in the energy absorbing material. It is believed that this absorbed energy is transferred to adjacent dermal tissue causing small disturbances in the dermal tissue. It is further believed that the disturbances are
10 repaired by a natural immune response of the skin creating new collagen fibers that provide added tension and elasticity to the skin section. In one embodiment, the energy absorbing material is graphite and the source of light is a Nd:YAG laser. The graphite may be deposited in the dermis in the form of a graphite thread, which can be sewn into the dermis. The graphite may also be deposited using tattoo techniques.

15 The details of one or more embodiments of the invention are set forth in the accompanying drawings and the description below. Other features, objects, and advantages of the invention will be apparent from the description and drawings, and from the claims.

DESCRIPTION OF DRAWINGS

20 FIG. 1 is a section of human skin with a cross section of one hair.

FIGS. 2A through 2F demonstrate a bleaching process. Each figure shows a successive diagrammatic view of a section of skin with hair immediately prior to being illuminated with a pulse of light energy.

FIG. 3 is a diagram of a laser apparatus for use during different processes
25 according to the invention.

FIG. 4 is a diagram depicting the paths of photons in a skin section during a typical bleaching process of the invention.

FIG. 5 is a graph of light transmittance plotted against beam diameter for different wavelengths of light.

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FIG. 6 is a diagram of a section of skin with three hairs.

FIG. 7 is a diagram of the section of skin of FIG. 6 with the hairs removed and the hair ducts filled with a clear fluid.

FIG. 8 is a diagram of a section of skin with three hairs removed from hair
5 ducts, the hair ducts being filled with a light absorbing contaminant for a hair removal process according to the invention.

FIG. 9. is a diagram of the section of skin of FIG. 8 after the contaminant has been caused to move to the bottoms of the hair ducts.

FIG. 10 is a diagram of the section of skin of FIG. 9 during illumination
10 with laser light according to the hair removal process.

FIG. 11 is a block diagram illustrating the arrangement of different layers of skin.

FIG. 12 is a diagram of the upper three layers of the epidermis of a section of skin during an initial step of a process to remove the stratum corneum.

15 FIG. 13. is a diagram of the section of skin of FIG. 12 during a process step in which ultrasound is applied to the section of skin to work a chromophore into spaces in the stratum corneum.

FIG. 14. is a diagram of the section of skin of FIG. 13 being illuminated.

FIG. 15 is a diagram of the section of skin of FIG. 14 during further
20 illumination.

FIG. 16 is a diagram of the section of skin of FIG. 15 after most of the layers of cells of the stratum corneum have been exfoliated.

FIG. 17 is a diagram of the upper body of a person illustrating placement of a transdermal drug delivery patch and an electronic sensor over two skin areas
25 from which the stratum corneum has been removed.

FIG. 18 is a block diagram of a time gated confocal microscope according to another aspect of the invention.

FIG. 19 is a graph that plots relative intensity of response to a signal reflected from a tissue specimen as a function of delay time.

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FIG. 20 is a diagram of a section of skin with one hair and illustrates a step in a process to deliver a composition containing a drug or active substance to the hair ducts according to another aspect of the invention.

FIG. 21 is a diagram of the section of skin of FIG. 20 illustrating a step in
5 which ultrasound is applied to urge the composition into the hair ducts.

FIGS. 22A-22E illustrate different types of biodegradable carriers for the composition illustrated in FIGS. 20 and 21.

FIG. 23 is a perspective view of a cooling apparatus according to another aspect of the invention.

10 FIGS. 24-28 illustrate other embodiments of a cooling apparatus.

FIG. 29 is a system for practicing a skin tightening method according to the invention.

FIGS. 30A through 30D illustrate steps in a facial skin tightening process.

FIGS. 30A and 30C illustrate a pattern of grid lines. FIGS. 30B and 30D
15 illustrate a graphite thread being inserted into the dermis in the pattern of the grid lines.

FIGS. 31A through 31F are diagrams of a section of human skin illustrating the results of illuminating a graphite thread within the dermis of the skin section.

FIG. 32A is an enlarged view of collagen fibers in a dermal layer. FIG.
20 32B is a similar view of a dermal layer with a graphite thread extending through the collagen fibers. FIG. 32C shows the results of illuminating the thread with light in a skin tightening procedure according to the invention. FIG. 32D shows the results of further illumination.

FIGS. 33A and 33B are drawings of a breast showing a grid line pattern
25 for a breast lift procedure according to the invention.

Like reference numbers and designations in the various drawings indicate like elements.

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DETAILED DESCRIPTION

OVERVIEW

Referring now to FIG. 1, a section of healthy human skin 11 includes a cross section of single hair 13. The surface of the skin 11 is composed of about 10-20 layers of dead and desiccated cells forming the stratum corneum 15. Below the stratum corneum 15 is the epidermis 17, and under that, the dermis 19 and subcutaneous basal cells 21. Hair 13 is rooted in the dermis 19 near basal cells 21, and includes a hair shaft 33, a hair duct 31, hair bulb 30, a nerve ending 34, a sweat gland 35, a sebaceous gland 38, arteries 36, veins 37 and a papilla 32. Melanocytes, which are interspersed among the basal cells of the hair bulb 30, have processes that extend into the matrix of the hair. Melanosomes containing melanin, a pigment, are synthesized and passed on to the hair-forming cells of the hair shaft 33, and so are responsible for hair pigmentation.

In some of the methods described below, such as hair bleaching and hair removal processes, it is important to apply laser energy very preferentially to the regions of the skin in and around the hair follicles and to avoid causing general damage to the skin tissue. For example, in hair bleaching processes, the follicles produce color in the hairs, *i.e.*, the melanin in the melanosomes. In general, skin tissue other than the papillae should not be damaged to any significant extent. To avoid unwanted thermal damage to skin tissue it is necessary that the light used to illuminate the skin be absorbed in a body that has a much greater absorption coefficient than that of skin at the wavelength used.

Absorption coefficients for melanin and for various tissue components have been measured and reported in the literature. In determining the wavelength of light to be used for processes of the invention, such as hair bleaching and for hair removal as described below, a second useful parameter to consider is the "photon path length," which is the inverse of the absorption coefficient. For each combination of absorbent (*i.e.*, melanin or other tissue component) and wavelength, there is a unique photon path length value. This value can be used to estimate the average distance a photon of a particular wavelength will travel through melanin or a skin component

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before being absorbed. In general, the shorter the photon path length, the greater the heat generated.

For comparison, estimates of the photon path length in melanin and various other skin components are given in Table 1 for photons from ruby, alexandrite, and Nd:YAG lasers, which produce a wavelengths in the range from about 0.694 to about 1.06 microns, respectively. The photon path length in the dermis for all three lasers is estimated to be in a range from about 3 to about 5 centimeters (30,000 to 50,000 microns). In the epidermis, however, photons of all three lasers are very readily scattered. Because of the scattering, the depth reached by a photon in the epidermis before its energy is absorbed is much smaller, typically only a few millimeters. As a result, most of the light beam energy is deposited in the skin in the form of heat between the surface and a depth of about 3 to 4 mm. For example, for photons having a wavelength in the range from about 0.6 to about 1.2 microns, the flux from laser illumination incident on the skin surface (the "incident flux") builds up at and just below the surface of the skin due to scattering of the photons by the skin tissue, but generally decreases with increasing depth. At depths in the range of 1 to 3 mm where most hair roots are located, the flux is about one half the incident flux.

TABLE 1

MEDIUM		PHOTON PATH LENGTH		
		Nd:YAG ($\lambda=1.06\mu$) (microns)	Alexandrite ($\lambda=0.755\mu$) (microns)	Ruby ($\lambda=0.694\mu$) (microns)
20	Epidermis	3,000	1,700	1,400
	Dermis	30,000	50,000	50,000
	Blood	500	2,500	1,400
	Melanin	100	70	50
	Graphite	0.1	0.098	0.097

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Melanin has a large absorption coefficient compared to the absorption coefficients of epidermis and dermis at wavelengths of light between about 500 nm and about 1500 nm. Accordingly, the estimated photon path length in melanin, as shown in Table 1, is between about 50 and 100 microns for photons of wavelength of about 0.694 to about 1.06 microns. Because it so readily absorbs light, the energy absorbed by melanin from light in this wavelength range is many times greater than that absorbed by skin tissue. For comparison it is useful to note that the photon path length in graphite is only about 0.1 micron. Thus, in general, the heat generated by illuminating a skin section having hair ducts containing melanin with light beams in this range of wavelengths is substantially less than that generated by the same light beam if the hair ducts contain carbon particles, but substantially greater than that generated in skin by passage of an incident light beam there through.

Skin tissue can be devitalized or damaged if heated to a temperature of about 70° C and maintained at that temperature for about 1 second. Higher temperatures can damage tissue in a shorter period, and temperatures between about 55° C and about 70° C for periods longer than 1 second can also damage tissue.

Heat energy diffuses relatively rapidly between light pulses, and the effects of each pulse is concentrated in regions of high photon absorption. In a rough estimation, 2×10^{-4} J of energy absorbed in a 100 micron diameter sphere of tissue would heat the sphere of tissue by about 90° C and that in about 0.01 seconds after illumination the heat energy would be dissipated over a 200 micron diameter sphere where the temperature increase would be down to about 10° C. In 0.1 second the heat would dissipate over a 300-400 micron diameter sphere and the temperature increase would drop to about 1°-3° C.

Several uses of laser light applied to the skin will now be described in detail. These include hair bleaching, hair removal, imaging subsurface skin structures, skin tightening, and preparing the skin for transdermal drug delivery and for measurement of body functions with skin sensors. Apparatus employed in these uses will also be described.

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No. 1: HAIR BLEACHING

Unwanted body and facial hair is an important cosmetic concern for many people. Many people wish to remove body hair that is dark, either black or dark brown. This has been historically true in modern times for leg hair and facial hair on women, and for body hair generally on certain male athletes, such as competitive body builders. More recently, many men have taken to removing body hair, such as the hair growing from their backs, to obtain a more youthful appearance. Waxing is uncomfortable and not very long-lasting. Electrolysis can be also painful, slow and expensive. Bleaching the hair provides an alternative that makes hair less noticeable, and for many people bleached hair is unobjectionable.

This aspect of the invention provides a process for bleaching hair shafts containing melanosomes below the skin surface, substantially throughout the lengths of the hairs below the skin surface, as well as above the skin surface. Since the hair is bleached below the surface of the skin, in some instances all the way to the root, a period of several weeks or months may pass before hair with darker color appears above the surface of the skin. The method is intended for use on healthy human skin for cosmetic purposes. The process generally does not cause significant or lasting harm to living tissues that surround the hairs.

As will be described in fuller detail below, the hair bleaching method of the invention employs a light source that is highly absorbed in melanin or in melanosomes containing melanin, and which will penetrate the skin reasonably well. In general, light with wavelengths between about 0.4 microns and about 1.5 microns will penetrate the skin and also be absorbed by melanin. To assist the light in reaching melanin located in portions of the hair shaft below the surface of the skin, the hair ducts are first filled with a fluid which is transparent to light at the wavelength being employed. The light is then directed at the skin in pulses having a pulse duration and fluence sufficient to destroy the melanin without causing significant damage to surrounding tissues. Light is transmitted through the fluid down the hair duct, and also scatters through the skin and thence to the hair duct, where it can penetrate the

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hair shaft and be absorbed by the melanin in the hair shaft. Light energy absorbed by the melanin causes the melanin to be destroyed, thereby bleaching the hair.

The first few pulses of light directed down the hair shaft into the hair duct and onto the skin surface contact melanosomes in the upper portions of the hair shaft so as to cause bleaching of the upper portions of the hair shaft. The bleaching of the upper portions permits additional photons to travel through the upper part of the hair duct to the lower portions of the duct, thereby bleaching the lower portions of the hair shaft. To obtain the most long-lasting results, the pulses of light are continued until the entire length of the hair shaft is substantially completely bleached.

There are two kinds of melanin in human hair: eumelanin and phaeomelanin. In general, black and brown hairs contain more eumelanin, while lighter colored hairs, such as red and blonde hairs, contain more phaeomelanin. White hairs have inactive melanocytes, which do not contribute melanin-bearing melanosomes to the hair root at all. It is not effective to attempt bleaching of "gray" hair that has become yellowed or otherwise discolored. Similarly, hair that has been artificially colored by a dye that absorbs light at a wavelength(s) other than those that are highly absorbed by melanin cannot be as effectively bleached using a light source that produces light highly absorbed by melanin. However, as one skilled in the art will appreciate, dye colors only the portion of the hair shaft above the skin surface. The method of hair bleaching disclosed herein can be used to bleach hair well below the skin surface, in some cases all the way to the hair root. Therefore, even artificially dyed hair that contains melanin in its natural state can be bleached at least below the skin surface using the method of this invention.

When light having a wavelength in the range between about 0.6 and about 1.2 microns is used to illuminate the skin surface, the light energy incident upon the skin surface is preferentially absorbed in melanin in hair ducts located at a distance of from about 3 to about 5 mm below the skin surface. The melanosomes containing the melanin are heated to a temperature sufficient to damage, disrupt or vaporize the melanosomes and/or tissue surrounding them without substantial damage to other skin tissue through which the light passes and is scattered. As described above, tissue is

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devitalized or damaged if heated to a temperature of about 70° C and maintained at that temperature for about 1 second. Higher temperatures can damage tissue in a shorter period, and temperatures between about 55° C and about 70° C for periods longer than 1 second can also damage tissue. Thus, the pulse duration, pulse repetition
5 rate and light fluence used in the hair bleaching procedure should be selected to avoid raising the temperature of skin tissues surrounding the hairs to these damaging ranges.

Refer now to FIGS. 2A-2F, which diagrammatically depict a section of skin 40 that contains a hairs 41, which are situated in respective hair ducts 42. Hairs 41 include melanosomes 43. FIGS. 2A-2F depict skin section 40 in a time sequence
10 wherein each figure immediately precedes skin section 40 being illuminated by a single light pulse. Although only one hair 41 is shown in FIGS. 2A-2F, it will be understood that several hairs similar to hair 41 can be growing in skin section 40, and that several hairs growing in a section of skin can be treated at the same time. Therefore, the following description will refer to a plurality of hairs 41 and associated
15 structures rather than to a single hair 41. In addition, similar features as shown in FIGS. 2A-2F will be referred to with the same reference numerals in subsequent figures of the Drawing.

Skin section 40 can be first washed with soap and water and then rinsed with water, and dried with a cloth towel. Skin section 40 can be further cleaned with
20 isopropyl alcohol or the like and allowed to dry.

To bleach hairs 41, a fluid 44 that is transparent to light, for example one that has an index of refraction substantially greater than that of skin tissue, which is about 1.37, is applied topically to skin section 40 with hairs 41 to be treated so as to cause fluid 44 to infiltrate into hair ducts 42 in skin 40. Fluid 44 should be transparent
25 to light at or near at least one frequency absorbed by melanosomes, but which penetrates skin a few millimeters. Any method can be used to enhance penetration of fluid 44 into hair ducts 42, such as, for example, gently rubbing skin 40 or employing ultrasound to work fluid 44 into hair ducts 42, and employing a surface active agent in fluid 44 to encourage penetration of fluid 44 into hair ducts 42 by capillary action.
30 However, care must be taken to avoid any technique that will irritate hair ducts 42. If

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hair ducts 42 become irritated, the sebaceous glands in the ducts will exude a wax-like substance that tends to plug hair ducts 42.

Preferably, transparent fluid 44 infiltrates throughout the entire length of hair ducts 42, but significant bleaching below the skin surface can also be achieved even when transparent fluid 44 does not infiltrate all the way to the bottom of hair ducts 42. If fluid 44 has an index of refraction substantially greater than 1.37, which is the index of refraction of skin tissue, the column of fluid 44 in each hair duct 42 conducts light similarly to an optical fiber. Light mineral oil has an index of refraction of about 1.47, which is significantly larger than the index of refraction of skin tissue. Therefore, a mineral oil-filled hair duct will conduct light as would an optical fiber. Light will reflect off the walls of hair ducts 42, but can penetrate into hair shafts 41, which will typically have an even higher index of refraction than fluid 44. The light penetrating hair shafts 41 can be absorbed by melanin in melanosomes 43 in hair shafts 41.

Fluid 44, such as mineral oil, is generously applied to skin section 40, for example, in a quantity of about one gram per 10 square centimeters. It is important that the oil infiltrate into hair ducts 42, preferably throughout their lengths. The oil can be massaged on the skin surface for a period of about 1 minute for each 10 square centimeters to encourage infiltration of the oil into hair ducts 42 in skin section 40. Skin section 40 can also be covered and allowed to rest for a few minutes after application of the oil before the illumination step commences.

After hair ducts 42 have been infiltrated with transparent fluid 44, skin section 40 containing the infiltrated hair ducts 42 is illuminated with short pulses of light that is well absorbed by melanin in melanosomes. The light must also be of a wavelength that is scattered by skin tissue, but which penetrates at least a few millimeters through skin.

Referring now to FIG. 3, an arrangement for applying pulsed light to skin section 40 is illustrated. A light source, such as a laser 50, provides pulses of light through a movable optic cable 51. The light pulses are emitted in a beam 52 through an endpiece 53, which is adapted to be held by the hand of an operator. Light beam 52

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is directed at skin section 40 and covers a spot 54 having a size that is smaller than skin section 40 but large enough to include more than one hair 41. The operator moves endpiece 53 to scan beam 52 over different areas of skin section 40.

Referring again to FIGS. 2A-2F, light beam 52 is directed towards the skin surface so that a portion of beam 52 is conducted through fluid 44 in hair ducts 42, and is absorbed by melanin in melanosomes 43 in hair shafts 41. Aiming the light beam about normal to the skin surface can help to direct the light into hair ducts 42 alongside hair shafts 41 through the transparent fluid 44 that fills ducts 42. These photons are internally reflected by the walls of ducts 42 and transmitted down ducts 42. A portion of these photons eventually are absorbed by melanin 43 in hair shafts 41. Due to scattering of the photons within the skin tissue, another portion of the light, which is transmitted to ducts 42 through the skin tissue, is also absorbed in melanosomes 43 in hair shafts 41. The light absorbed by melanin in hair shafts 41 imparts sufficient energy to melanosomes 43 to damage, disrupt and/or vaporize them, thereby bleaching hair shafts 41.

Although beam 52 is applied in a direction such that portions of the beam enter the surface openings 45 of ducts 42, most of the photons in beam 52 are incident on the skin surface, pass through the epidermis of skin section 40, and scatter. The first pulse is typically absorbed in the upper portions of hair shafts 41. This causes bleaching of the upper portions of hair shafts 41, indicated in FIG. 2B by a decrease in melanosomes 43 in the upper portion of hair shafts 41. It is believed that the bleaching of the upper portions decreases absorption in these regions and permits additional photons to travel to the lower portions of ducts 42. As the hair shafts 42 are bleached near the skin surface, the absorption in the hair shafts 42 is greatly reduced in the bleached regions, permitting photons from subsequent pulses to travel deeper into ducts 42. Fluid-filled ducts 42 conduct light similar to optical fibers. The deeper penetrating photons bleach successively lower portions of hair shafts 41, illustrated in FIGS. 2C-2F. Regions of hair shafts 41 that have been bleached appear to scatter light with greater efficiency. The process is continued until hair shafts 41 are substantially completely bleached (FIG. 2E). The number of pulses needed to completely bleach a

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hair depends on the fluence and wavelength of the light. The higher the fluence, the fewer pulses are needed.

Clinical tests using mineral oil infiltrated into hair ducts between the outside walls of hair shafts and the inside walls of their respective hair ducts have
5 confirmed the bleaching process as depicted in FIGS 2A through 2F. These tests have also confirmed that unless oil is infiltrated into the hair ducts, bleaching generally occurs only in a region of the hair shafts above the skin surface.

Transparent fluids that are useful in the practice of this invention include any light mineral oil, NF, such as DRACOL™ 5 to 13, or transparent gel lubricants,
10 many of which may contain surface active agents that help the fluid infiltrate the hair duct. Fluids other than mineral oil can also be employed, such as, for example, baby oil, peach oil, and tea tree oil, so long as the index of refraction of the fluid exceeds that of skin tissue.

FIG. 4 diagrammatically depicts photon absorption in a section of skin 40.
15 Photons A, D and E that are incident on the surface of skin 40 scatter in skin 40, and are ultimately absorbed in skin tissue at respective locations A', D' and E' distant from hair shaft 42. Photon B scatters in skin 40, and is absorbed in a melanin granule 43B in hair shaft 41. Photon C travels partially down hair duct 42 through mineral oil 44, and is absorbed in a melanin granule 43C in hair shaft 41. Photon F travels all the
20 way down hair duct 42, and is absorbed in a melanin granule 43F in the bulbous portion of papilla 46.

Thus, bleaching of hair shafts 41 and papillae 46 is obtained by absorption of photons from two sources—those photons transmitted through fluid 44 in ducts 42 and those photons scattered through the skin which eventually reach the hair shafts 41
25 and papillae 46. The combination of the two processes enables use of lower beam fluences than would otherwise be necessary were ducts 42 not filled with high index of refraction fluid 44.

In general, the above considerations show that light at a wavelength of between about 0.4 microns and 1.5 microns will penetrate skin tissue reasonably well,
30 and be reasonably well absorbed in melanin in melanosomes. This frequency band

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extends into both the visible and near infrared ranges of the electromagnetic spectrum. Especially good transmission in skin is obtained with wavelengths between 0.6 microns and 1.3 microns. Short pulses of light having sufficient energy to disrupt or vaporize the melanosomes are used. The pulse duration should be shorter than the thermal relaxation time of melanin, which is about 1 μ s. The beam fluence should be in a range of about 0.1 J/cm² to about 10 J/cm², but this can vary depending on the wavelength of light used.

The beam diameter should be large enough to obtain deep penetration of light into the skin. Refer now to FIG. 5, which graphically plots the transmittances of collimated light at different wavelengths through skin tissue *in vivo* as a function of incident beam diameter. The skin type used was Caucasian male, the anatomic site was skin tissue located between fingers, and the tissue thickness was about 3.4 mm. The graph shows that the transmittance generally increases with increasing wavelength, and for each wavelength, increases with increasing incident beam diameter up to about 8-12 mm before beginning to level off. Therefore, the beam diameter should be about 8-12 mm.

Any type of light having a wavelength in the range from about 0.4 micron to about 1.2 microns, including that provided by a high intensity lamp, is highly absorbed in melanin, yet is well scattered in skin tissue. Therefore any source that produces light having a wavelength within this range can be used in the practice of this invention. Appropriate filters can be used to select desired wavelengths. Many other wavelengths of light could be utilized so long as the light penetrates skin fairly well and also is reasonably well absorbed in melanin. The preferred sources of light are alexandrite, ruby and Nd:YAG lasers, which provide light having a wavelength in the range from about 0.694 μ m to about 1.06 μ m. Experiments utilizing each of these three laser light sources are described in the Examples below.

Example 1 - Alexandrite Laser

In this embodiment, an alexandrite laser 50 operates at a wavelength of .755 micron with a beam cross sectional area of about 0.5 cm². Controls on laser 50

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permit adjustment of pulse duration as short as 0.5 ns at low pulse power using a Q switch and a longer pulse duration of greater than 100 μ s in a non-Q switch mode. Pulse energy can be adjusted to between 0.01 J and 5 J. Alexandrite lasers meeting these specifications are available from Light Age, Inc. of Somerset, New Jersey.

- 5 As discussed above, the illumination should be sufficient to achieve hair bleaching without significantly damaging surrounding skin tissue. A pulse duration of about 10 ns, pulse energy of 1.2 J, beam cross sectional area of about 0.8 cm², and repetition rate of about 1-10 Hz provides beam 52 with a pulse intensity, or fluence, of about 1.5 J/cm². Beam 52 scatters well and is absorbed relatively poorly in skin tissue. How-
10 ever, substantially all of the beam energy is ultimately absorbed in the skin between the surface and a depth of about 0.5 cm. Each section of skin is illuminated for about six or so pulses.

- With the illumination parameters given above, about 12 J of energy is delivered to a skin section of 0.8 cm² in one second. while most of the illumination
15 energy will be absorbed, some will also be reflected from skin 40. There is very little general heating of skin 40. Skin to a depth of about 0.5 cm is heated by about 10° C above normal skin temperature, or to about 33° C. At this temperature, the skin hardly begins to feel warm, and there is no pain and no significant damage to skin 40.

- There are about 2×10^{18} photons in a 1 Joule pulse of light at a wavelength
20 of 0.755 micron. If, for example, the cross-sectional area of the beam incident on the skin is 0.5 cm², and the opening of the hair duct is only about 0.00008 cm², then about 3×10^{14} photons enter directly into the hair duct. Therefore, about 1.5×10^{-4} Joule of energy enters the hair duct, and this is sufficient energy to increase the temperature of a 100 micron sphere of tissue (about the size of a papilla) to about 75° C.

25 **Example 2 - Ruby Laser**

Another embodiment of the present invention utilizes a ruby laser, which produces a laser beam having a wavelength of about 0.694 micron. The beam from a ruby laser is absorbed about twice as efficiently in melanin, and about four times more efficiently in the blood of the tiny blood vessels of the papillae, as is the beam

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from an alexandrite laser. Ruby lasers are commercially available. This embodiment employs a 10 mm diameter beam at a beam pulse energy density, or fluence, of about 1 J/cm², using a 10 ns pulse at a frequency of 10 pulses per minute. Up to about 20 pulses can be provided to a skin section before allowing the skin to cool down. This is
5 more than sufficient in most cases to effect bleaching of the hair 41.

Example 3 - Nd:YAG Laser

A Nd:YAG laser can also be used for practicing this invention. Photons produced by a Nd:YAG laser, which has a wavelength of about 1.06 micron, are more readily absorbed in blood, but less readily absorbed in melanin than are those from an
10 alexandrite laser. Absorption in melanin is only about 40 percent that of a ruby laser. Nd:YAG lasers are commercially available from many sources. Effective hair bleaching is obtained employing a pulse duration of about 10 ns, a beam diameter of about 10 mm, and a beam pulse fluence of about 2 J/cm². Only a few pulses should be necessary to effect bleaching.

15 Additional pulses may be provided to deliver light energy to the melanin in the papillar region. If there is sufficient melanin or other absorbers in the papillar region, it may be possible to deliver sufficient energy there to damage the hair and inhibit or prevent future hair regrowth. For this purpose it is important to use light at a wavelength that will provide high absorption in the papillar region. In addition, longer
20 pulses of light with higher beam fluences can be used to thermally damage papillae, as described in the following examples. These beams generally do not cause explosion of the melanosomes in the papillae, as the energy is transmitted over a time period greater than the thermal relaxation time of the melanosomes. However, energy from photon scattering through skin tissue proves a sufficient boost to energy
25 absorbed in melanin from photons traveling down the hair duct to damage the papillar region sufficiently to reduce future hair growth.

It is important that the hair ducts remain open and unobstructed during illumination. For some subjects, it may be necessary to stretch the skin in at least 3

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directions in order to assure that the hair ducts remain open from the skin surface to the papillae during illumination.

As described above, the photon flux is highest very near the skin surface due to light scattering in the epidermis and dermis. As a result there is preferential
5 heating in the skin at its surface, as compared to deeper layers of the skin. This heating is undesirable, and can be controlled by cooling the skin surface, either prior to or during the illumination, or both. Methods of cooling the skin surface can include, but are not limited to, direct or indirect application of rapidly flowing ambient air, cold air, compressed nitrogen, or ice packs. One method is to use a
10 chilled fluid, such as cold mineral oil, in the process described above and to reapply chilled fluid periodically during the process.

Different types of cooling apparatuses that can be employed in conjunction with this hair bleaching process and other processes that illuminate the skin with laser light are described in greater detail below in Section 7 with reference to FIGS 23-28.
15 These cooling apparatuses generally include a transparent sapphire window that is placed in contact with the skin during illumination. The window is supported by a structure that includes a heat exchanger, and that provides a passage for light to pass through the window to the skin underneath. Heat from the skin is absorbed by the window and removed from the window by the heat exchanger.

20 In this aspect of the invention the goal is to bleach hair rather than to remove it or substantially inhibit its growth. One advantage of using the described short-pulse light parameters to bleach hair is that the bleached condition is not permanent. As the treated hairs continue to grow, new melanosomes will be generated, and the new growth of hair will revert to a natural hair color. The natural
25 reversibility of the bleaching process is particularly desirable among males who may wish to bleach their facial hairs to avoid the need to shave daily, but who do not want to permanently lose the ability to grow a beard, should they desire to do so.

Another advantage is that hair is bleached below the surface of the skin, so that a colored portion of the hair will not be visible until new growth emerges from
30 the skin surface. The regrowth can then be bleached to remove its color before it

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emerges from the skin surface. By repetition of the bleaching process at spaced intervals of a few weeks, the problem of "dark roots" showing at the base of the bleached hairs can be eliminated.

In addition, the laser conditions required to bleach hair are generally
5 milder than those used to hinder hair growth, so there is less risk of damage to skin tissue in laser hair bleaching than in laser hair removal procedures.

No. 2: HAIR REMOVAL USING TRANSPARENT FLUID IN EMPTY HAIR DUCTS

Another way to deal with unwanted hair is to destroy the hair so as to
10 inhibit its regrowth. This aspect of the invention provides a method for the permanent or long term removal and inhibition of regrowth of unwanted human hair. In this method, hair growing in hair ducts in a section of skin is first extracted, for example, by waxing. Then, a fluid is infiltrated into the empty hair ducts in the section of skin. The fluid is substantially transparent at a frequency band of light that will penetrate at
15 least a few millimeters through skin tissue and that is at least reasonably well absorbed in a naturally occurring chromophore, such as, for example, melanin or blood. The fluid should also have an index of refraction that is greater than that of skin tissue. Then, the section of skin is illuminated with a beam of light at the frequency band, the beam being directed such that portions of the beam enter fluid-filled surface
20 openings of hair ducts in the skin section. A small portion of the beam enters the ducts and is transmitted through the transparent fluid to the papillae where a substantial portion of it is absorbed in the naturally-occurring chromophores. The major portion of the beam scatters in the skin tissue. This causes general heating of the skin tissue, including skin tissue in the regions of the papillae.

25 The illumination is limited so as to avoid general overheating of skin tissue. In this embodiment, the skin is heated generally to temperatures in the range of about 40° C to 48° C, which is close to but below the pain threshold and also below the damage threshold for skin tissue. The melanin, blood cells or blood vessels, or other naturally occurring chromophores of the papillae preferentially absorb the

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photons traveling down the hair shafts. The illumination is chosen to raise the temperature of papillae to at least about 70° C with each pulse of light. This is generally sufficient to devitalize papillar tissue. There is no significant damage to skin tissue other than tissue in the immediate vicinity of the papillae. The skin section can
5 be allowed to cool down before repeating the illumination. By also actively cooling the skin, either during illumination and/or between illumination pulses, a greater amount of light energy can be applied to destroy papillae by absorption of the light in the chromophores without excessively heating the skin. The illuminating and cooling can be repeated several times to devitalize the hair.

10 In one aspect of this hair removal process, long pulse laser energy is applied in a manner so as not to vaporize the melanin in the melanosomes in the papillar region. Light with wavelengths of between about 400 nm and about 1500 nm can be used. Wavelengths between about 600 nm and about 1300 nm appear to work best. The pulse duration should be longer than the thermal relaxation time of the
15 naturally occurring absorber, such as blood vessel in the papillar region or melanin. The pulse duration can range between about 100 μ s and about 200 ms, and a pulse duration in the range of about 10 ms to about 100 ms is best. The beam diameter should be large enough to obtain beam penetration through the skin that is deep enough to reach the bottoms of the papillae. Such beam diameters can be in the range
20 of about 8 mm to about 12 mm. The pulse energy density, or fluence, is high enough to thermally denature tissue surrounding the natural follicular absorbers, such as the melanin or blood vessels. These fluences can be in a range of about 3 J/cm² to about 300 J/cm².

Merely vaporizing the melanin in the hair shaft or papilla normally does
25 not significantly damage the skin's ability to grow hair. As described above in Section 1, vaporizing the melanin in melanosomes bleaches the hair and the hair can continue to grow. If the bleached hair falls out or is pulled out, it is quickly replaced by another hair from the same papillae. In the presently described method, on the other hand, heat is applied relatively more slowly to the skin. This takes advantage of the natu-
30 rally occurring absorber's relatively high absorption of skin penetrating photons. Care

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is taken to not heat the melanin to temperatures high enough to merely cause bleaching.

Alternatively, the illumination can be applied with shorter pulses, with pulse durations in a range between about 5 ns to about 50 ns, but with sufficiently high intensity pulses to vaporize or otherwise utterly destroy or damage the natural absorber, and with enough energy to cause more extensive damage to surrounding tissue than in the bleaching process. These pulses are much shorter than the thermal relaxation time of, for example, melanin. When applying short pulses of light, the fluence should be in a range of between about 0.1 J/cm² to about 10 J/cm², and more preferably between about 1.5 J/cm² to about 5 J/cm². The beam diameter should be between about 8 mm and 12 mm. The mechanism of damaging or destroying the viability of hairs is different from the first described method. Instead of generally heating the papillar region, the violent destruction of the absorbers causes damage to nearby regions around the papillae. Because hairs are first removed, the illuminated photons are not absorbed by the hairs before they can reach the papillar region.

These hair removal methods are similar to the above-described hair bleaching method in that a transparent fluid having an index of refraction that is greater than that of skin tissue is used to help conduct light in hair ducts. It is the combination of damage caused by light transmitted down through the fluid and by light scattered by through skin tissue that ultimately devitalizes the hairs. In the long pulse, thermal method, general heating of the skin tissue by light scattered through the tissue is combined with more intense heating of the papillar region by light transmitted down the ducts through the fluid. In the short pulse regime, it is more likely that the papillar regions are damaged by exploding or vaporizing absorbers in the papillar region that absorb photons transmitted through the ducts and scattered through the skin tissue.

Referring now to FIG. 6, a section of skin includes three hairs growing in hair ducts. Hairs grow from follicles, which extend partially up through ducts from respective bulbous regions at the base of hairs. Skin section can be first washed with soap and water, then rinsed with water, and dried

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with a cloth towel. Skin section can be further cleaned with isopropyl alcohol or the like and allowed to dry.

The next step is to physically remove hairs 41 from hair ducts 42 in skin section 40. This can be done by using a commercially available hair removal wax product, for example, NATURE'S OWN PINE WAX™, which is marketed by Select Spa Source of Sausalito, California. The waxing procedure recommended by the manufacturer should be followed. Referring now to FIG. 7, waxing removes many hairs 41 completely, however, some of hairs 41 break off above the hair root and are only partially removed, as shown by the middle hair 42. Some hairs, such as hairs which did not extend beyond the surface of skin 40 prior to the waxing step, may remain intact after waxing. The partially removed and intact hairs may require a second treatment at a later date.

Next, mineral oil 44, or another transparent fluid with an index of refraction that is greater than that of skin, is topically applied to skin section 40. Oil 44 is applied in quantities of about 0.1 gram/cm². Oil 44 is massaged thoroughly on the skin surface for a period of about one minute to cause as much of the oil as possible to infiltrate into hair ducts 42 in skin section 40. It is believed that in most cases oil 44 penetrates to the bottoms of hair ducts 42. FIG. 7 shows hair ducts 42 filled with oil 44.

The next step is to illuminate skin section 40 with pulses of light at a wavelength that is well absorbed by one or more naturally occurring chromophores in follicles 46 or in tissue 48 surrounding and nourishing follicles 46. Such light absorbent chromophores can be melanin or hemoglobin, however, the invention is not limited to these two chromophores. The light used should also penetrate well through skin.

Light can be applied with a beam 52 produced by a laser 50, as shown in an arrangement similar to that illustrated in FIG. 3. The light producing arrangement in this hair removal method differs from that shown in FIG. 3 in that skin section 40 has hairs 42 removed before light is applied. Laser 50 provides pulsed coherent light

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through movable optical cable 51. Pulsed light beam 52 emerges through endpiece 51, which is held by an operator.

As indicated above, the present invention provides a process of illumination with the objective of achieving maximum destruction of hair growing potential with minimal damage to skin tissue in general. Specific examples of embodiments employing light with different characteristics will now be described in detail.

Example 4 - Long Pulse Alexandrite Laser

In this example, the illumination is provided by an alexandrite pulsed laser operating at a wavelength of 0.755 micron with a beam diameter of about 10 mm, providing a cross sectional area of about 0.8 cm². Controls on the laser permit selection of pulses as short as 0.5 ns at low pulse power using a mode-locked Q switch and a long pulse duration of greater than 100 microseconds in a non-Q switch mode. Pulse energy can be adjusted to between 0.01 J and 5 J. Alexandrite lasers meeting these specifications are available from suppliers such as Light Age, Inc. with offices in Somerset, New Jersey.

The objective is to heat the skin tissue of the papillar area to temperatures high enough to prevent hair growth. We target papillae 46 in skin section 40 and skin tissue 48 within a distance of about 100 to 200 microns immediately surrounding papillae 46. We select pulse duration of 100 ms, a beam cross section of 0.8 cm², a repetition rate of up to about 5 HZ, and a pulse intensity or fluence of about 80 Joules/cm². The 0.755 micron beam is scattered very well and absorbed relatively poorly in skin tissue. However, substantially all of the beam energy entering the skin is ultimately absorbed in the skin between the surface and a depth of about 0.5 cm. Each section of skin section 40 is illuminated for about 1 to 5 pulses. About three pulses are typically sufficient to devitalize hairs 41. Beam 52 is aimed to direct the maximum possible portion of beam 52 into the openings at the tops of hair ducts 42, understanding that this is still a very small portion of the total energy in the beam. Most of the beam passes through the epidermis into the dermis of the skin and heats

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the skin in general. Three pulses, of about 80 Joules/cm² each, deliver about 240 J/cm² into the skin.

This energy input is large enough to cause general damage to skin tissue. Therefore, the illuminating should only be done while steps are taken to cool the illuminated section of skin. A cooling apparatus, such as any one of the devices illustrated in FIGS. 23-28, can be used to help cool the skin during illumination. With active cooling, the skin can begin to feel warm but there will be no damage to the skin and normally no pain. If the cooling is insufficient or too much illumination is applied, the subject can experience pain before the illumination causes general damage to the skin tissue. Subjects should be instructed to let the laser operator know if the subject feels pain and in such event the operator should stop the illumination of that skin section immediately.

A portion of pulse laser beam 52 is transmitted down hair ducts 42 through transparent mineral oil 44 that fills ducts 42. For beams 52 directed at skin section 40 in a direction approximately parallel to the axis of hair ducts 42, we estimate that about 50% to about 70% of the light incident on the openings of ducts 42 may be transmitted to papillar areas 46 at the bottom of the duct. Mineral oil has an index of refraction of 1.47 which is larger than that of skin tissue, which is 1.37. The mineral oil 44 filled hair ducts 42 will conduct light somewhat like optical fibers as indicated in FIG. 4, but without scattering or absorption by hairs 41 within ducts 42.

The papillar area 48 of the skin of many people contains an abundance of melanin and small blood vessels which absorb 0.755 micron light substantially better than dermal tissue in general. The combined result of photons transmitted down hair ducts 42 and photons scattering through skin section 40 to the papillar regions 48 is a substantial preferential heating of papillae 46 and surrounding skin tissue 48 in the immediate vicinity of papillae 46. We estimate the total temperature rise in and immediately around the papillae to be in the range of about 30° C to about 90° C during each of the 100 ms pulses. Each pulse independently causes damage to the hair. These pulsing temperature increases are in addition to a smaller, more wide-spread temperature rise due to scattering and absorption of light in skin section 42 and

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can damage tissue in the papillar region 48 sufficiently to prevent or inhibit hair regrowth.

A very important element to the present invention is the control of energy input to the skin tissue. As indicated above the skin cannot be generally heated above about 65° C for even one second without risk of general damage of the skin tissue. The tissue in and immediately around papillae 46 should be heated at the proper rate. If heat is applied too slowly, heat will dissipate to other regions and tightly controlled preferential tissue destruction will not be possible. The 100 ms pulses are long enough that the melanin in the melanosomes of papillae 46 can dissipate heat to the surrounding tissue 48 in the region of papillae 46 as the energy is being absorbed so that the temperature of the melanosomes does not reach an explosive temperature. This means that after allowing skin section 40 a few minutes to cool down the process can be repeated with additional damage to the papillar area. The process can be repeated about 6 to 10 times, allowing at least about 3 minutes for each skin section 40 to cool down before repeating the treatment of the same skin section 40. Using a cooling device also helps to keep the temperature of the skin within a safe range.

A single 10 nanosecond pulse above about 2.5 to 4 Joules/cm² would likely explode the melanosomes which in effect bleaches the tissue containing the melanin so that the absorption of additional energy is greatly reduced. The quick bleaching of the tissue usually does not appreciably damage the tissue. If such short pulses are used they should preferably be used as the last phase of the illumination phase of the process.

Because the photon flux is highest very near the skin surface, there is preferential heating at the surface as compared to deeper layers of the skin. This preferential heating can be countered somewhat by cooling the surface either prior to or during the illumination. Methods of cooling include use of rapidly flowing ambient air, cold air, compressed nitrogen and ice packs. One method is to use cold mineral oil in the process described above and to replace it periodically during the process. Skin section can also be actively cooled by employing a heat exchanger having a light-transmitting window on skin section 40 during illumination. Embodiments of suitable

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heat exchangers are described in greater detail in Section 7 below. Employing an active heat exchanger can allow more light energy to be applied to skin section 40 without causing general damage to the skin.

Example 5 - Long Pulse Ruby Laser

5 Another embodiment of this hair removal method utilizes a laser which produces a 0.694 micron wavelength laser beam 52. This wavelength is absorbed about twice as efficiently in melanin and about four times more efficiently in the blood of the tiny blood vessels of the papillar region as compared to the 755 nm wavelength alexandrite laser beam. Ruby lasers produce light at this wavelength and
10 are commercially available. For this wavelength of light, a pulse fluence of about 60 J/cm², a pulse duration of about 100 ms, a beam diameter of about 10 mm, at a frequency of about 10 pulses per minute are illumination characteristics that should be effective for removing hair. As with the long pulse alexandrite laser beam, about 1-5 pulses are usually sufficient to devitalize or otherwise damage the hairs.

Example 6 - Long Pulse Nd:YAG Laser

15 The Nd:YAG laser can also be used for practicing this invention. The absorption of its 1.06 micron photons in blood is better than that for the alexandrite beam. Nd:YAG lasers are available from many sources. The laser can be operated to provide 120 J/cm² pulse fluence with a 100 ms pulse duration and a 10 mm beam
20 diameter. These beams should not cause explosion of the melanosomes in the papillae, but energy absorbed in the papillar melanin and blood vessels from photons traveling down the hair duct through the transparent mineral oil, combined with energy absorbed from photons scattering through the skin tissue, is sufficient to cause sufficient damage to the papillar region to satisfactorily reduce future hair growth.
25 About 1 to 5 pulses are applied to each region of skin section 40 to cause such damage.

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Example 7 - Short Pulse Alexandrite Laser

In this mode, the alexandrite laser is operated with a beam pulse fluence of about 3 J/cm², a beam diameter of about 10 mm, and a pulse duration of about 10 ns. About 1-5 pulses are needed to cause sufficient damage to the papillar region to
5 devitalize the hair or otherwise inhibit its regrowth.

Example 8 - Short Pulse Ruby Laser

The ruby laser is operated with a beam pulse fluence of about 2 J/cm², a beam diameter of about 10 mm, and a pulse duration of about 10 ns. About 1-5 pulses are needed to cause sufficient damage to the papillar region to devitalize the hair or
10 otherwise inhibit its regrowth.

Example 9 - Short Pulse Nd:YAG Laser

The Nd:YAG laser is operated with a beam pulse fluence of about 4 J/cm², a beam diameter of about 10 mm, and a pulse duration of about 10 ns. Again, about 1-5 pulses are needed to cause sufficient damage to the papillar region to devitalize the
15 hair or otherwise inhibit its regrowth.

For some subjects it may be helpful to stretch the surface of the skin in at least 3 directions in order to assure that the hair ducts remain open from the skin surface to the papillae. Instead of removing the hair from the skin section with wax, a depilatory could be used or the hairs could be extracted by plucking. Depilatories
20 normally dissolve the portion of the hair above the skin surface and for about 1 mm below the surface. This would leave a large percentage of the hair shaft intact within the duct. However, for some subjects who object to the pain associated with the wax treatment, this could be a preferred method of practicing the invention. After the depilatory step the remainder of the process is as described above with a mineral oil
25 application and illumination to devitalize the hair.

To improve transmission through the hair duct with portions of the hair remaining in the hair duct, it is suggested that only one or two very short, high energy pulses be used to bleach the melanin in the hair shaft to reduce absorption in the hair

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shaft. This could permit subsequent long pulse beams to travel down the duct to the papillar region. The challenge is to bleach the melanin in the hair shaft without bleaching the melanin in the papilla.

- Many other frequencies of light could be utilized; however, preferably the light used should penetrate skin at least fairly well and also be reasonably well absorbed in the tissue in the papillar region. Any of the frequencies between those frequencies corresponding to wavelengths of 0.4 microns and 1.5 microns should work to some degree, but the 0.6 to 1.2 micron window is preferred. This invention is not restricted to laser beams. For example, high intensity lamps could be used.
- Appropriate filters could be used to select desired wavelengths. Many fluids other than mineral oil will work. As indicated above, preferred fluids will have an index of refraction greater than that of skin tissue, which is about 1.37. Other preferred fluids specifically include baby oil, peach oil and tea tree oil.

No. 3: HAIR REMOVAL WITH HAIR DUCTS ACTING AS LIGHT PIPES

- This method of inhibiting growth of hair from papillae located at the bottoms of hair ducts in a section of skin is similar in most respects to that described above in Section 2. In that method, naturally occurring chromophores were used as light absorbent materials to absorb energy from light applied to the skin. In this method, however, a light-absorbent contaminant is introduced into hair ducts after hairs are removed from section of skin. Methods of hair removal using a contaminant and laser light are described in U.S. Patent Nos. 5,226,907 and 5,425,728.
- Referring now again to FIG. 6, a section of skin 40 includes hairs 41 growing in hair ducts 42. The method first includes the step of removing hairs 41 from respective hair ducts 42 in section of skin 40, for example, by waxing. FIG. 8 shows section of skin 40 with hairs 41 substantially removed. At this stage, a contaminant 49 is applied to skin section 40.

Contaminant 49 has a high absorption at or near at least one frequency band, or wavelength, of light. Contaminant 49 can include carbon particles mixed with a liquid, such as mineral oil, peach oil or the like. As shown in FIG. 8, contami-

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nant 49 is initially confined to the upper reaches of ducts 42. At least a portion of contaminant 49 is then caused to move to the bottoms of ducts 42, as shown in FIG. 9. Contaminant 49 can be moved downwards with a variety of methods, which can include gentle massaging and applying ultrasound to the skin. Contaminant 49 can also be caused to move toward the bottoms of ducts 42 by applying a few pulses of laser light to skin section 40, wherein the laser pulses are of a duration, frequency and fluence to drive contaminant 49 farther into ducts 42. If contaminant 49 is carbon particles mixed with oil, forcing pulses 55 of light at 1064 nm wavelength produced by a ND:YAG laser, having a pulse duration of about 10 ns and a fluence of about 3 J/cm², will be absorbed by the carbon particles. The light energy absorbed from forcing pulses 55 causes the carbon particles to fracture into smaller fragments with a force sufficient to drive some of the fragments deeper into ducts 42. Only a few forcing pulses 55 are typically needed to drive the carbon particles farther into the bottoms of ducts 42, as shown in FIG. 9.

15 An arrangement for applying a pulsed beam of laser light to skin section 40 is illustrated in FIG. 3 and described in Sections 1 and 2. In this method, however, hairs 41 are first removed from skin section 40.

Now referring to FIG. 10, hair ducts 42 are then filled with a light guiding fluid 44 having an index of refraction that is greater than that of skin tissue. A region of skin section 40 is then illuminated with a light beam 52 at the wavelength which is absorbed by contaminant 49. In the case where contaminant 49 includes carbon particles, the Nd:YAG laser can be used again. Fluid 44 conducts light down hair ducts 42 to contaminant 49. The paths of photons in ducts 42 are indicated with lines 56. Contaminant 49 absorbs energy from the illuminating light and transmits at least a portion of the absorbed energy to papillae 46 at the bottoms of respective hair ducts 42, thereby damaging or destroying papillae 46 with the transmitted energy. Where carbon particles are the contaminant, several more short light pulses similar to driving pulses 55 can be applied at the end of the process to further fragment any remaining particles into insignificant sizes.

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The opening of a hair follicle has the shape of a convex lens. Therefore hair follicles 46 will focus light once they are filled with high refractive index fluid 44, such as mineral oil. By this means, a complete "fiber optic" light guiding system is formed naturally. Hair-removal can be achieved employing both long pulse
5 duration light and short pulse duration light, as will be described in the examples below. Since the light from beam 52 is guided to papillae 46 through hair ducts 42, rather than propagated through tissue, the light source can be of any wavelength that is highly absorbed by contaminant 49.

In the case in which contaminant 49 is carbon particles, the following
10 illumination parameters have been found to be useful in destroying papillae 46 after the carbon particles are driven to the bottoms of ducts 42. The illuminating wavelength should be in a range of about 400 nm to about 1500 nm, however, wavelengths in a range between about 600 nm and about 1300 nm are more effective. The diameter of beam 52 should be large enough to obtain deep penetration of the skin, for exam-
15 ple, in a range of about 8-12 mm diameter. Although contaminant 49 does not need to absorb photons scattered through the skin for this method to be effective, using an illuminating wavelength having good penetration through skin will help avoid excessively heating near the surface of skin section 40. Damage can be caused to papillae 46 by either heating the carbon particles with long pulse illumination or by
20 fragmenting the carbon particles by exploding them with short duration pulses, as described in the examples below.

Example 10 - Short Pulse

The pulse duration should be shorter than the thermal relaxation time of the contaminant. The contaminant in this embodiment includes carbon particles that
25 have a thermal relaxation time on the order of a microsecond. Therefore, a pulse duration of about 5 ns to about 50 ns can be used, and a duration of about 10 ns is very effective. We use a Nd:YAG laser that produces pulsed light at a wavelength of 1064 nm. The beam fluence for each pulse should be enough to explode or fragment the carbon particles. A fluence in a range between about 0.1 J/cm² and about 10 J/cm²

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will work, and a fluence of about 3 J/cm^2 works well. Using these pulse parameters and a beam diameter of about 10 mm, about 5-10 such pulses are enough to damage or destroy the papillae so as to inhibit the regrowth of the hair.

Example 11 - Long Pulse

5 This embodiment employs illumination pulses with a duration that is longer than the thermal relaxation time of the contaminant so that the contaminant heats up sufficiently to denature papillar tissue. In this example, where the contaminant includes carbon particles and the light source is a Nd:YAG laser producing pulsed light at a wavelength of 1064 nm, the pulse duration is in a range of about 100
10 μs to about 100 ms, and the beam fluence can be in a range of about 3 J/cm^2 to about 60 J/cm^2 . In a specific embodiment, the beam diameter is about 10 mm, the fluence is about 40 J/cm^2 , and the pulse duration is about 100 ms. With these parameters, about one to five pulses are sufficient to effect hair removal.

15 **No. 4: REMOVAL OF THE STRATUM CORNEUM TO CREATE A BIOLOGIC WINDOW FOR TRANSDERMAL DRUG DELIVERY AND MEASUREMENT OF BODY FUNCTIONS**

 A method is described for selectively removing the stratum corneum of the skin to create a portal for transdermal drug delivery and for measurement of body functions. The stratum corneum is widely recognized as the key barrier against
20 effective drug delivery across the intact skin. Removing the cellular layers of the stratum corneum before applying a transdermal drug delivery system would enhance the ability of a drug to diffuse across the remaining layers of the skin. The stratum corneum also acts as a resistive barrier to electronic sensors that are placed on the skin for measuring body functions, such as sensors used for taking electrocardio-
25 grams. Removing the stratum corneum would enable more sensitive and accurate electronic sensing of a medical patient's body functions.

 The epidermis of the human skin includes several distinct layers of skin tissue. These layers are shown in block diagram form in FIG. 11. The deepest layer is

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the stratum basale, which consists of columnar cells. The next layer up is the stratum spinosum, which is composed of polyhedral cells. Cells that are pushed up from the stratum spinosum are flattened and synthesize keratohyalin granules to form the stratum granulosum layer. As these cells move upward they lose their nuclei and the
5 keratohyalin granules fuse and mingle with tonofibrils. This forms a clear layer called the stratum lucidum, which is composed of closely packed cells. These cells are further compressed as they move up, forming opaque squama. Squama are all flattened remnants of cells that have become completely filled with keratin and have lost all other internal structure, including nuclei. These squama constitute the outer
10 layer of the epidermis, the stratum corneum.

At the bottom of the stratum corneum the cells are closely compacted and adhere to one another strongly, but closer to the surface they become loosely packed and eventually flake away at the surface. In the cheek skin of a 50 year old person, the outer portion of the stratum corneum typically consists of about 15 layers, which flake
15 away at a rate of about one or two layers per month.

The stratum corneum cells are lifeless. Nerve endings and blood vessels do not extend into the stratum corneum. The purpose of the stratum corneum is to provide the skin an outer barrier to environmental hazards. The stratum corneum also serves as a barrier to transdermal drug delivery systems, such as, for example,
20 nicotine patches.

This aspect of the invention uses laser light to remove some or all of the stratum corneum. Stripping the external 10-20 layers of the stratum corneum off the skin can expose the underlying basal surface of the epidermis. Application of a transdermal drug delivery system directly to the denuded skin decreases the distance
25 across the epidermis and bypasses the key barrier to passive diffusion.

The procedure for removing the stratum corneum includes treating the skin with carbon particles such that the particles infiltrate into spaces between the cells in the upper few exposed layers of the stratum corneum, and irradiating with laser light at a wavelength that is readily absorbed by the carbon particles. When short duration
30 pulses of light are used, the particles quickly absorb sufficient energy to cause them

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make tiny explosions that exfoliate about 1-6 surface layers stratum corneum cells. This process of exfoliating the outer layers of the stratum corneum is described in U.S. Patent No. 5,423,802. The process can be repeated to remove additional layers of the stratum corneum. This creates a "denuded window" in the treated section of skin
5 through which a drug or other active agent can be transdermally delivered. The size of the denuded window may be tailored to the dimensions of a transdermal dressing or patch.

Referring now to FIG. 12, a section of the outer three layers of the epidermis, the stratum corneum 61, the stratum lucidum 62 and the stratum granulo-
10 sum 63, is diagramed in sectional view. There are spaces between some of the cells in the stratum corneum. A mixture of carbon particles 65 and an oil or lotion is applied to the surface of the stratum corneum. Carbon particles 65 can be approximately 1 micron graphite particles suspended in baby oil in a 20-50% carbon to oil weight ratio.

15 The next step is to force carbon particles 65 into spaces 64 located between stratum corneum cells. This step is shown in FIG. 13, in which an ultrasound unit 66 operating at about 0.2 W/cm² and about 10 MHz is employed to infiltrate carbon particles 65 into spaces 64. Approximately five minutes of ultrasound treatment at this frequency and power level will force a significant number of carbon
20 particles 65 down through several layers of the stratum corneum 61.

The next step is to provide pulses of laser light to the treated section of skin. An arrangement for scanning pulsed laser light to a section of skin is illustrated in FIG. 3. In that system, laser 50 provides pulses of light through movable optical cable 51. A pulsed beam 52 is emitted through end piece 53, which can be held by an
25 operator. The operator moves endpiece 53 while aiming beam 50 at a subject's skin 40 to scan beam 53 over a selected area.

In the described embodiment, the laser system can be a SOFTLIGHT® system, supplied by ThermoLase Corporation of San Diego, California. Laser 50 in this system is a Q-switched Nd:YAG laser providing pulsed light at a wavelength of
30 1064 nm. Beam 50 should be large enough to provide good penetration of skin, with a

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diameter of between about 8-12 mm. In the described embodiment, a beam diameter of about 8 mm is employed. The fluence of beam 50 should be in a range of about 0.1 J/cm² to about 10 J/cm². A fluence of about 3 J/cm² works very well. The pulse duration is in a range of about 5 ns to about 50 ns, with a duration of about 10 ns
5 providing good results.

Referring now to FIG. 14, laser beam 52 is scanned over the section of skin treated with carbon particles 65 such that each location of a selected area is subjected to pulses at a frequency of about 1 Hz. A first pulse of beam 50 is primarily absorbed by a surface layer 67 of carbon particles 65. The light energy is deposited
10 more quickly than heat can be dissipated from particles 61. Enough energy can be absorbed by particles 65 to cause them to vaporize the smaller ones of particles 65 and/or explode the larger ones of particles 65 into smaller fragments that fly off with high energy. Lower layers of carbon particles under surface layer 67 are effectively shielded from the first pulse by surface layer 67. However, the destruction of surface
15 layer 67 helps to force more carbon particles 65 deeper into the stratum corneum 61. Scanning beam 52 over the section of skin is repeated until all carbon particles 65 on the skin surface are vaporized or otherwise blown away. Eventually, beam 52 penetrates to carbon particles 65 located in spaces 64, causing these particles 65 to vaporize or explode as shown in FIG. 15. This process loosens and breaks off cells 68
20 from the stratum corneum 61. Scanning continues until almost all remaining carbon particles 65 are destroyed.

Typically, the entire process will exfoliate about 1 to about 6 layers of the stratum corneum. More carbon particles 65 can be applied to the same section of skin and all the steps repeated to exfoliate additional layers of cells from the stratum
25 corneum 61. FIG 16 illustrates a section of skin in which almost all layers of the stratum corneum 61 have been removed by the described process. The stratum lucidum 62 remains essentially intact.

Once several layers of the stratum corneum 61 are removed from a section of skin, a drug or other agent, or an electronic sensor can be applied to that section in
30 a well-known manner. Referring now to FIG. 17, the upper body of a male subject is

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illustrated. A transdermal delivery skin patch 69 is placed on the subject's upper arm over an area of skin 70 that been treated as described above to remove essentially all of the stratum corneum 61. FIG. 17 also illustrates the placement of an electronic sensor 71 in the subject's chest for sensing electric signals from the heart. Sensor 71 is positioned over a second area of skin 72 from which the stratum corneum 61 has been substantially removed. Each of patch 69 and sensor 71 can be attached to the subject's skin in any manner that is usually used in the art. In the case of patch 69, the drug or active agent that patch 69 carries is delivered through skin area 70 more effectively than it would through an untreated nearby area of the skin. In the case of sensor 71, sensor 71 is able to receive a stronger electronic signal through skin area 72 than would be possible in untreated areas of the subject's skin.

Removing some or all of the layers of the stratum corneum 61 is not painful. The described process removes only dead cells and is substantially harmless to layers of living cells in the skin located below the stratum corneum.

This aspect of the invention includes all methods of laser removal of the stratum corneum, including as well the use of chromophores other than carbon particles 65, as well as any laser based approach, without restriction, that can be used to safely remove the outer 10-20 layers of the stratum corneum. Instead of a patch, a lotion or cream can be used containing the active agent, for instance encapsulated for slow release in a slow release drug delivery formulation, such as liposome, microcapsule or other lipid-based systems.

No. 5: TIME RESOLVED CONFOCAL MICROSCOPE FOR IMAGING OBJECTS THROUGH HIGHLY LIGHT SCATTERING MEDIA

This aspect of the invention provides an instrument for noninvasive microscopic observation of objects embedded deep in a highly light scattering media, for example biologic tissues, with spatial resolution of the order of less than one micron in both axial and radial directions. The instrument combines a confocal microscope with optical ultrafast time resolution techniques. The combination of

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these techniques in a single system can provide a significant improvement in the signal to noise ratio of a confocal microscope.

A confocal laser scanning microscope (CLSM) is an instrument designed to construct three-dimensional images of microscopic objects in weakly scattering media. The principles of operation for confocal microscopes are known, and will not be discussed in detail. It suffices to mention that confocal microscopes scan an illumination beam from a point source over an area of a sample while an objective lens focuses the illumination beam at a fixed depth in the sample. The reflected signal is received by an optical signal detector, such as a photomultiplier tube (PMT), that has a small aperture placed in front of its receiving surface. The aperture in front of the detector cuts off out of focus light scattered from areas of the sample other than the location being scanned. If a collimated light source is used instead of a point source, a second focusing lens positioned in front of the detector aperture lens focuses the signal from the sample onto the detector receiving surface through the aperture. By recording the signal from the PMT as the illumination beam is scanned over a plane of the sample, an image of features of that plane can be constructed. By moving the focal depth with the objective lens, images of slices of the sample at different depths can be obtained. The CLSM offers high spatial resolution and fine sectioning capabilities. Image sections can be obtained by confocal microscopy that are separated by less than one micron. Conventional confocal microscopes also provide a high image signal to background noise ratio (SNR). This results from the excellent spatial resolution that can be obtained with a confocal microscope and from the predominance of single light scattering over multiple scattering in a specimen object. The high resolution is a combined effect of sharp focusing of a probe beam into the object and high spatial resolution of an optical sensing system.

When an object is viewed through a layer of turbid media, the quality of the images is determined by the capability of an optical system to do two things. The first factor is the optical system's ability to collect a sufficient amount of signal light scattered by the object directly into the system without any further scattering in the surrounding turbid medium. The second factor is the optical system's ability to reduce the effect of

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- light responsible for the noisy background detected by the system from the scatterers dispersed in the out of focus volume. As multiple scattering becomes more and more significant, the signal to noise characteristics of the conventional confocal microscope imaging system deteriorate because scattering snatches photons from the main stream of the focused laser beam and the signal level decreases. Simultaneously, the background of diffusely scattered light increases. The image signal becomes indistinguishable for a reasonable signal accumulation time when optical inhomogeneity of the medium is significant enough for a few scattering events to occur, on average, during light travel through the layer.
- 10 A conventional confocal microscope, though having high spatial resolution in the axial direction (depth), is ineffective for providing reasonable images below 200-300 micron deep into human tissues, *e.g.*, skin. Photons emerge from the tissue after reflection deep in the tissue. A photon that penetrates deeply into tissue before scattering is more likely to be absorbed before it has a chance to emerge from the
- 15 tissue than a photon that scatters near the surface. Thus, the expected signal from deeper depths within the tissue is much lower than that from structures closer to the surface. Up to 50% of light incident on human skin is diffusely scattered back and much of this light is due to the photons that leave the tissue after a few scattering events. In CW illumination mode, these short-travel-time-in-tissue photons are
- 20 responsible for superficial glare that dominates the weak image signal coming from deeper within the tissue. In addition, the reflected signal is spread out over time. Promptly reflected photons that travel a short path length in the tissue are reflected first and more deeply penetrating photons that travel a longer path length emerge later.
- 25 The invention significantly improves the ratio of an image signal to a background noise signal when objects hidden in highly light scattering media, such as skin tissue, are observed with a confocal microscope. As mentioned above, the invention incorporates optical ultrafast time resolution techniques with a confocal microscope. This improves signal-to-noise characteristics of the confocal microscope, and enables
- 30 visualizing deeper structures in the scattering media than would be possible using

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only a confocal microscope. The principle concept of time resolved confocal microscopy is to employ a time gating method to prevent the photons that are promptly reflected from near the surface of a sample, which constitute the bulk of a signal reflected from tissue, from affecting formation of the image being obtained from

5 deeper in the sample in the confocal microscope.

To image deeply embedded structures in human skin the following factors are combined:

1. Making use of the sharp focus response and low out-of-focus wings of resolution characteristic of the confocal microscope;
- 10 2. Employing light having good penetration in skin tissue for imaging, such as light in the 700-1200 nm range of wavelengths, and particularly IR light in a range of approximately 750 nm - 1000 nm; and
3. Increasing the effective penetration depth of probing radiation by selecting for imaging only multiply scattered light with long transient time within
- 15 the tissue by employing a time-resolving technique.

Time resolved optical imaging is a technique that includes illuminating an object with a short laser pulse and time gating the scattered light received back from the object.

The range to a light scattering object is determined by the delay between the gate position in time with respect to the moment of the pulse emission. The range is one
20 half of the round trip distance of light within the delay time. In general terms, spatial resolution of the time ranging system becomes better as the probing pulse becomes shorter and as the time gate used for detecting the reflected light from the object becomes narrower. For ultrafast pulses, for example, 100 fs pulses, the potential range resolution is of the order of 20 microns in skin tissue, which has an index of refraction
25 of about 1.4. A delay line is employed to adjust the gate position with an accuracy of a few femtoseconds using off-the-shelf optical components and translation stages.

The signal-to-noise characteristics of the ranging system depends on how much light is reflected by the object and how much background light fits within the same time gate. As short light pulses propagate through a turbid medium their intensities are
30 reduced by light scattering. The propagating laser beam also generates a diffuse glare

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in the medium, much of which contributes to the background noise signal. Without time gating, one would detect a short signal pulse reflected by the object and a much longer pulse due to the multiple scattering of light by spatially distributed inhomogeneities in the background. In highly scattering media the intensity of the signal

5 component is low and the integral intensity of the background is high. On the other hand, the noise component is by far more extended in time as a result of multiple scattering. With a narrow time gate the level of this noise component constitutes a fairly small fraction of its integral intensity.

Several methods are known for implementing optical time gated detection. Various
10 techniques for time-resolved transillumination imaging are reviewed in "Time Resolved Transillumination Imaging," by R. Berg, *et al.*, in Medical Optical Tomography: Functional Imaging and Monitoring, SPIE Proc., vol IS11, pages 397-424 (1993), the entire disclosure of which is included herein by reference. Any of the devices and methods disclosed by Berg, *et al.* can be incorporated, with some
15 modification within the skill of persons in the optical imaging arts, in the time gated confocal microscope of the invention. One group of incoherent time gating methods take advantage of nonlinear optical effects in materials, such as, for example, the Kerr effect, second harmonic generation, and the like. A powerful control pulse opens the gate within an ultra short time interval to let a much weaker signal of interest to pass
20 through and be detected. Another group of incoherent methods incorporates electronic detection with a short reference pulse synchronizing a photon counting correlator or an ultrafast streak camera.

In coherent time gating methods, ultrashort reference pulses are made to interfere with a certain portion of the signal, which has been broadened by multiple scattering.
25 The interference produces a heterodyne signal at a photodetector proportional to the product of electric vectors in both pulses within the time of duration of the reference pulse. To facilitate detecting the heterodyne component of the signal and to improve its noise characteristics the reference wave is phase modulated, the AC signal of the photodetector is separated with an electronic filter and its amplitude is measured to
30 retrieve information about the signal wave intensity.

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- Referring now to FIG. 18, a time gated confocal microscope (TGCM) system 100 includes a modified confocal laser scanning microscope (CLSM) system 102. The essential components of a CLSM system that can be employed with the described TGCM system 100 can be a type OZ system, produced by NORAN Instruments Inc. of Middleton, Wisconsin, and which is set to operate in the reflected light mode. CLSM system 102 includes a beam scanner 103, a photomultiplier tube (PMT) detector 104, a confocal aperture 105 positioned in front of PMT detector 104, a PMT signal preamplifier amplifier (AMP1) 106 and a second amplifier (AMP2) 107 that includes a band filter with the central frequency of the band corresponding to the oscillation frequency of a phase modulator 108, as will be described in greater detail below. An objective lens 109 focuses light from beam scanner 103 onto a specimen 110. An acousto-optic deflector in the Y direction in beam scanner 103 is replaced by a galvanometer scan mirror similar to that scanning in the X direction in the same device.
- The light source for CLSM system 102 is a femtosecond laser 111. In the described embodiment, laser 111 is a Tsunami type laser that is pumped by an argon laser 112, both being the products of Spectra-Physics Lasers, Inc., of Mountain View, California. Laser 111 produces 80 fs pulses of light at a wavelength of 750 nm, an average power of about 500 mW, and a pulse frequency of 82 MHz.
- TGCM system 100 also includes an optical delay line 113 and reference beam phase modulator 108. Delay line 113 includes a one direction manual translator 114 having a resolution of 1 μm or better, and two broadband cone reflectors 115, 116. Modulator 108 includes a broadband 100% reflecting mirror 117 attached to an oscillating piezoelectric actuator 118.
- Femtosecond pulses 125 from laser 111 are fed into CSLM system 102 through one of its standard ports. A 50/50 beam splitter 119 replaces one of the standard corner reflectors between the port and the first scanning mirror (not shown). Light passing through beam splitter is scanned in X and Y directions in a plane perpendicular to the beam by beam scanner 103 and focused at a selected depth in specimen 110 by lens 109. Reflected light collected from specimen 110, which is broadened due to scatter-

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ing in specimen 110, propagates through the modified optical system of the microscope, and is directed by beam splitter 119 as a signal pulse 126 onto the built-in PMT 104. A standard filter in front of the face of PMT 104 is replaced by a filter 120 adapted to pass through light of 750 nm wavelength and to reject other background
5 wavelengths.

The other portion of light pulse 125 from laser 111 that is directed by splitter 119 to optical delay line 113 becomes a reference pulse 127. Delay line's 113 purpose is to compensate for the difference in the optical paths between the light propagating in the imaging portion of the device and the light propagating in the reference signal
10 portion. Fine tuning with the help of translation stage 114 enables the short reference pulse 127 to interfere with a certain part of the broad signal pulse 126.

The relative timing of signal pulse 126 and reference pulse as they are directed towards PMT 104 is indicated by the diagram immediately to the right of filter 120 in FIG. 18. Reference pulse 127 strikes PMT 104 at the same angle as signal pulse 126.
15 The two pulses 126, 127 interfere at the face of PMT 104 to give rise to a cross interference component in the PMT signal. Optical phase modulator 108 in the reference arm of TGCM system 100 introduces a periodic phase modulation into reference signal 127. This causes the PMT signal to be periodically amplitude modulated. The band filter in AMP2 107 separates out the amplitude modulated
20 signal. The amplitude of this component is then measured and converted to a brightness signal 122 of the image pixel corresponding to a particular location of the microscope sampling volume. A reference beam attenuator 121 can be used to optimize the signal to noise ratio of the PMT signal.

It is important that the time gating of the imaging signal be synchronized with the
25 spatial location of the microscope sampling volume. When reference pulse 127 opens the gate the reflected light must be coming exactly from the focus of the microscope to combine spatial and time gated discrimination of the images. As discussed above, when femtosecond laser pulse 125 is incident onto a highly scattering specimen 110, reflected light from specimen 110 is primarily due to photons traveling different paths
30 in the tissue. In the case of multiple scattering in the tissue, the distribution of the

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travel times of the photons broadens the reflected pulse, which becomes signal pulse 126.

FIG. 19 plots a calculated typical backscattered light time response of a semi-infinite light scattering phantom media having an index of refraction of about 1.4 to an ultrashort pulse illumination. Zero time is the moment of incidence of a 100 fs pulse on the phantom surface. The phantom has a scattering coefficient of 50 cm^{-1} , an absorption coefficient of 1 cm^{-1} , and an asymmetry factor (g) of 0.9. The narrow region at a delay time of about 10 ps indicated by reference number 128 represents the fraction of the backscattered light detected with a 100 fs incident pulse and a 10 ps delay of the gate.

Signal pulses 126 make a round trip to the focus of the microscope and back in a time $\tau = 2*Z_f/V$, where Z_f is the depth of focus from the surface of the media and V is the speed of light in the media. When the delay time is chosen to be equal to this round trip time both the confocal and the time gating system work synchronously, enabling the best spatial resolution and signal to noise performance of the system. For example, if the focus is located at a depth of 1 mm and the refraction index of the medium is 1.4, the time delay must be about 8.5 ps for the optimum performance of the microscope.

The principle benefit of the TGCM system is that it is able to image subsurface structures at depths several times deeper than previously attainable with convention confocal microscope systems. In addition, the TGCM system provides excellent resolution, even at tissue depths of about a millimeter or more.

A further advantage of the described imaging system is that it employs non-ionizing radiation, which can be harmful to the skin and underlying tissues.

Another advantage of the present system is that different types of subsurface structures can be imaged by employing different wavelengths of illuminating light.

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**No. 6: METHOD FOR DEPOSITING SUBSTANCES INTO THE HAIR
SHAFT CANAL**

This aspect of the invention provides a device and methods for depositing medications and other active substances into the hair shaft canal to create a local accumulation of the drug or active substance for slow release of a constant low dose. The invention can be employed, for example, to introduce a substance for regulating hair growth or for regulating the activity of sebaceous glands.

The principle methods presently used for hair growth regulation include hormone therapy, vasodilation with minoxidil, immunomodulation with cyclopropane, treatment with antibodies, or hair grafting. These techniques can involve a long term treatment regimen with drug administration or topical application more than once a day, or hair transplant operations.

Referring now to FIG. 20, a section of skin 40 includes a hair shaft 41 growing in and extending from a hair duct 42. It will be understood that other hair shafts 41 can be growing from hair ducts 42 in skin section 40. According to this aspect of the invention, substances that regulate hair growth or the activity of sebaceous glands are deposited in hair duct 42 encapsulated in microspheres formulated to have slow release properties. A substance, such as a drug, is encapsulated within or bound to the microspheres. Microspheres appropriate for use with the invention include liposomes, coacervate drops, erythrocyte shadow, latex or gelatin spheres, carbon microcrystals, and the like. A suspension 80 of the drug or substance, or a combination of drugs and/or substances, in the form of microspheres is topically applied to an area of skin to be treated, including skin section 40, the area of skin including one or more hair duct canals. Suspension 80 can be rubbed in and then the excess wiped off the skin surface 81 in order to create a concentration of the spheres around hair shafts 41 at the entrances to hair ducts 42.

Referring now also to FIG. 21, an ultrasonic device 82 or other mechanical oscillating device can also be applied to skin surface 81 to provide mechanical pulses that encourage the microspheres to enter into the hair canals.

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The size of microspheres can be in a range of about 100 nm to about 2 μ m. The stratum corneum serves as a barrier to intradermal penetration of these size microspheres through skin surface 81, and then to the hair shafts. The walls of hair shafts 42 are lined with cells that do not provide such a barrier. The drug delivery thus
5 is very localized inside hair ducts 42. In addition, drug delivery is very effective within hair shafts 42 because of the lack of a transdermal barrier there.

The membrane of the microspheres is biodegradable, so that the encapsulated drug or active substance starts being delivered some time after suspension 80 is deposited.

The drug or active substance is then released slowly as the microspheres degrade. If
10 the size and/or type of the microspheres administered in a single application is varied, the microspheres will decay and begin to release the encapsulated or attached substance at different times. In addition the amount of drug or active substance released by different types or sizes of microspheres will also vary. As a result, the method of the invention can be tailored to bathe the papillae with the drug or active
15 substance over an extended period of time.

Referring now to FIG. 22A, a multilayer liposome 83 has an active substance 84 encapsulated therein. FIG. 22B illustrates an erythrocyte shadow 85 with medication 86 inside. FIG. 22C shows a coacervate drop with a drug 88 inside. FIG. 22D illustrates a latex sphere with monoclonal antibodies 90. FIG. 22E depicts crystal
20 particles 91 with drug molecules 92 bound to them.

No. 7: COOLING WINDOW FOR USE WITH LASER SKIN AND HAIR PROCESSES

Some of the processes described above apply pulses of laser light to the skin to bleach hair, to remove hair, to exfoliate layers of the stratum corneum and to image subsur-
25 face structures. It is important to keep the section of skin being illuminated with laser light cool enough so that the skin tissue is not denatured or otherwise damaged. Some locations may experience intense heating, such as the papillar regions in some hair removal processes, but the surrounding skin tissue should not be heated to a temperature over about 45° C for any extended period of time.

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This aspect of the invention provides a cooling apparatus that can be used to help remove heat from the skin during illumination with laser light. Referring to FIG. 23, a cooling apparatus 200 includes a window 202 that is substantially transparent to light at the wavelength of the laser. In the described embodiment, window 202 is made of sapphire, which has good thermal properties. Window 202 is cooled by a support structure 204 that includes a heat exchanger 206. Support structure 204 preferably is made of a good thermal conductor, such as OFHC copper, and includes a hollow annular space 208 that is filled with a reservoir of cooling fluid 210, such as water. An inner wall 212 of annular space also forms an outer cylindrical wall of an open cylindrical space 214 through which laser light passes to window 202. One or more cooling elements 216 are attached to an outer wall 218 of annular space 208. Cooling elements 216 can be cooling fins, or, as in the embodiment illustrated in FIG. 23, they can be thermoelectric cooling elements. Cooling fluid 210 may circulate by convection. In the embodiment illustrated in FIG. 23, water is circulated by miniature fans 220 that are powered by a power supply (not shown). A temperature sensor 222 may be positioned in cooling fluid 210 or otherwise thermally coupled to support structure 204.

In use, cooling apparatus 200 is placed over the section of skin being illuminated such that only window 202 is in contact with the skin. A transparent thermally conductive gel (not shown) may be applied to the skin to facilitate thermal contact between the skin and window 202. Examples of thermally conductive gels include No. 5 Afterwax Skin Gel, produced by L'ELYSCE LABS, Aloe Vera with Lidocaine, available at Thrifty Payless stores, Corn Huskers lotion, produced by Warner-Lambert, and K-Y Jelly, produced by Johnson & Johnson. When laser light is directed through window 202, the section of skin in contact with window 202 is cooled by window 202.

Another embodiment of a cooling device 230 is illustrated in FIG. 24. Cooling device 230, like cooling device 200, includes a sapphire window 202 in good thermal contact with a support structure 232, and an annular space 208 with a fluid reservoir 210. Fans 220 stir cooling fluid 210. A temperature sensor 222 senses the temperature of cooling fluid 210. A second sensor 224 senses the temperature of window 202. An

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end of support structure 232 opposite window 202 includes an array of circumferentially spaced thermoelectric cooling elements 234 attached thereto. Thermoelectric cooling elements 234 support and are thermally coupled to an annular ring-shaped radiator 236.

- 5 Yet another embodiment of a cooling device 240 is illustrated in FIG. 25. Cooling device 240 is substantially the same as cooling device 230, but does not include annular space 208 or a reservoir for cooling fluid 210, and therefore is much shorter than cooling devices 200 and 230. Cooling device 240 includes a support structure 242, thermoelectric cooling elements 234 and a radiator 236.
- 10 A fourth embodiment of a cooling device 250, shown in FIG. 26, includes a support structure forming an annular-shaped space 208 for chilled cooling fluid 210. Annular space 208 includes a cover 252. Chilled cooling fluid flows through an inlet tube 254 that passes through cover 252 and terminates in a ring-shaped portion 256 positioned close to window 202. Ring-shaped portion 256 of inlet tube 254 includes apertures
- 15 256 through which chilled cooling fluid 210 flows to fill annular space 208. Cooling fluid 210 flows out via an outlet tube 259 that passes through cover 252.

Referring now to FIG. 27, yet another embodiment of a cooling apparatus 260 includes a window 202, an annular-shaped support structure 262, but no fluid reservoir or thermoelectric cooling elements. Instead, support structure 262 is

20 wrapped with coils of tubing 264 through which chilled water or another cooling fluid 210 circulates. Tubing 264 includes an inlet tube 266 and an outlet tube 268. Chilled cooling fluid 210 is pumped from a chilled reservoir 269.

FIG. 28 shows still another embodiment of a cooling apparatus 270. Cooling apparatus 270 includes a sapphire window 202 held at the bottom end of a substantially

25 annular-shaped support structure 272. An upper end of support structure 272 includes a first annular-shaped flange 274 that extends radially outward. Flange 274 is coupled to an array of solid state cooling devices 276, which are powered by a power supply 279. A second annular shaped flange 278 is coupled to the top ends of cooling devices 276. Support 272 and flanges 274, 278 are fabricated of a good thermal conductor,

30 such as copper.

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**No. 8: SKIN TIGHTENING SYSTEM AND PROCESS WITH LASER
LIGHT**

As humans age, their skin becomes thinner and less elastic. Sagging skin around the face and breasts is often an objectionable part of aging. Since many individuals want to remain young looking, face lifts for men and women and breast lifts for women are popular to those who can afford the cost. The present invention, through absorption of light energy, provides a tool for greatly simplifying breast lifts and face lifts, thereby making these procedures more economical.

FIG. 29 shows a system 310 for increasing the tension and elasticity in a section of human skin 311, including an energy absorbing material 312 disposed in the skin at a distance "d" from an illumination source 314. An energized light beam 316, preferably a laser beam, is emitted from source 314. Beam 316 spans the distance d and imparts energy to the energy absorbing material 312, which can be graphite in a thread or a particulate form. As will be described in greater detail below, it is believed that with a judicious choice of energy absorbing material 312 and illumination, illuminating energy absorbing material 312 causes such material to absorb energy, some of which is transferred to surrounding skin tissue. The transferred energy causes disturbances in the skin. The body's natural healing response then creates more collagen fibers in the region of the disturbances, thereby strengthening and tightening the skin.

Graphite is a good choice for the energy absorbing material because it has a three dimensional crystal structure that is strong in two directions and weak in the third direction. Accordingly, graphite thread is weak in a direction transverse to the longitudinal direction of the thread. The illumination energy source can thus break particles of graphite from near the thread's outer periphery.

A useful thread for embodiments of this invention is a thread comprised of about 30 strands of graphite fibers, each fiber having a diameter of about 10 micron. This type of thread can have a diameter of about 50 microns. A good light source 14 is a laser, for example an Nd:YAG laser. Graphite is strongly absorptive of the 1064 nanometer (nm) wavelength beam produced by the Nd:YAG laser, the absorption being more

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than 4,000 times greater than the absorption of this wavelength by human skin tissue.

The penetration of the beam into solid graphite is in the range of 1 micron.

While not desiring to be limited to any particular theory of operation, it is believed that the invention operates in accordance with certain physical principles described

- 5 now. When graphite thread is illuminated from one side with 10 nanosecond (ns), 3 J/cm² Nd:YAG pulses at a wavelength of 1064 nm, the surface atoms to a depth of about 1 micron are heated to the vaporization temperature of graphite which is 3,600° C and a tiny but powerful explosion occurs on the surface layer. On a microscopic level, fragments of the surface of the thread disperse and travel away from the thread.
- 10 It is further believed that if the thread is embedded in dermal tissue and illuminated as described above with about 3 J/cm² 10 ns Nd:YAG pulses, the fragments will fly off through the dermal tissue and come to rest at distances from the thread of up to 500 microns, about 100 microns being the average travel distance. The fragments impact and damage skin tissue cells. The fragments dispersed from the thread are typically
- 15 very hot (*e.g.*, temperatures in the range of about 3,000° C). Accordingly, heat is transferred to surrounding tissue. On the average a one micron size particle (10⁻¹² cm³) of graphite at about 3,000° C will carry about 10⁻⁸ J of heat energy. This is a very small quantity of energy, but there are many thousands of small micron size particles exploded off the graphite thread with each pulse and they are spread over distances
- 20 ranging out to about 500 microns from the position of the thread. These hot, high energy fragments cause damage to the dermal tissue creating a long, very thin wound in the dermal tissue below the epidermis.

- The skin of the face and breasts is about 2 mm thick. The epidermis is a thin (about 0.4 mm) outer layer of the skin and is composed primarily of layers (about 30) of cells
- 25 which are produced by cell division at the lower levels of the epidermis and move up and into the stratum corneum over a period of about 45 days, becoming more compacted and flatter on the way. By the time the cells reach the stratum corneum, they are dead and are regularly flaked off.

- The strength and flexibility of the skin is provided by the lower thicker layer of skin,
- 30 the dermis, which includes blood vessels, sweat glands, sebaceous glands and hair

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follicles. A primary component of the dermis is a matrix of collagen fibers. These fibers are about 15 microns wide and relatively long. The collagen fibers are arranged in a three-dimensional, relatively randomly woven pattern. This pattern permits the skin to be stretched by distances of a few percent upon the application of a very small
5 force. However, once the skin is stretched to the extent that the fibers making up the dermis become aligned roughly parallel to each other, further stretching force is resisted very strongly by the fibers. When the stretching force is removed the skin rebounds with the fibers resuming their three-dimensional, relatively random pattern. A typical collagen fiber is made up of several hundred small fibrils. These fibrils are
10 about 0.1 micron wide that are, in turn, made up of individual molecules called tropocollagen molecules. The tropocollagen molecules are made up of three polypeptide chains, each having a helical structure. Together, the three chains form a super-helix. Unlike the cells making up the epidermis, the collagen fibrils of the dermis are not living cells, but are produced by living cells in the dermis called fibroblasts. As
15 we grow, the fibroblasts produce the dermal fibers as needed. When skin is damaged, fibroblast cells migrate to the site of the wound and initiate the production of new fibrils which combine to form new collagen fibers.

The dermis also includes a material called "ground substance," which fills spaces between the collagen fibers. Ground substance functions as a lubricant, allowing the
20 collagen fibers to slide past each other. It is also thought that the ground substance functions as a pathway for diffusion of nutrients through the skin and to assist the fibroblast cells in creating new fibers.

Another component of the dermis is a network of elastic fibers which constitute about 2 to 4 percent of the total volume of the skin. These fibers are also, like the collagen
25 fibers, produced by fibroblast cells. However, these fibers are comprised of elastin and are interwoven with the collagen fiber network and add greatly to the elastic properties of the skin.

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Example 12 – Face Lift Procedure

A typical face lift tightens sagging facial skin by removing a portion of the sagging skin. The remaining skin is stretched to cover the space previously covered by the removed section so that some of the sag of the skin is eliminated. Incisions are usually
5 made in hair-covered areas so that the resulting scar is not apparent. Current face lifting procedures have many adverse consequences including long periods of recovery after the treatments. In some cases, after the painful procedures and the long recovery times, the patient is disappointed with the results.

The present invention improves on surgical face lift procedures by eliminating the
10 need to surgically remove skin tissue. Referring now to FIGS. 30A and 30D, grid lines 320 are drawn on the facial skin 322 of a patient at the beginning of the procedure. On each cheek grid lines 320 are about 1 inch apart and generally horizontal and vertical. Under the chin grid lines 320 are about 1/2 inch apart, six lines side to side and 7 lines front to back. A graphite thread 324 is then sewn through the dermis
15 below grid lines 322 as shown in FIGS. 30B and 30C. Graphite thread 324 is implanted under skin 320 at a depth which is as close as possible to the middle of the dermis layer of the skin. FIG. 1B shows the position of a needle 326 used for inserting one of the vertical threads 324 in the right cheek of the patient. FIG. 1C shows needle 326 positioned for threading one of the side to side threads 324 under the chin. FIG.
20 31A shows a cross section of facial skin 322, which includes the dermis 328, the epidermis 330 with the stratum corneum 331 at the surface, and a layer of fat 332 below the dermis 328. Graphite thread 324, also shown in cross-section, is positioned about centrally in dermis 328.

FIG. 32A is a representation of the collagen fibers 334 in skin tissue. Note that many
25 of the individual fibers 334 are bundled into larger fiber bundles 336. FIG. 32B is a representation of a graphite thread 324 sewn into the dermal collagen fibers 334. Once graphite threads 324 are in place, they can be illuminated. In the described embodiment, threads 324 are illuminated with approximately 10 nanosecond light pulses produced by a Nd:YAG laser, the pulses having a fluence of about 3 J/cm². A
30 pulse rate of 10 Hz can be used, and the beam can be scanned slowly along grid lines

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320 so that each section of skin 11 receives about four pulses at the 10 Hz rate. A fluence of about 3 J/cm² appears to provide sufficient energy to heat the skin enough to raise its temperature a few degrees but not enough to cause any general skin damage other than in the immediate vicinity of the graphite thread.

- 5 It is believed that absorption of the light pulses by graphite thread 324 causes tiny explosions in the thread's strand layers. FIG. 31B and FIG. 32C both show the result of one pulse. Note that graphite fragments 338 are now distributed over a volume about 100 to 500 microns from graphite thread 324. Note also in FIG. 32C some damage has been created in some nearby collagen fibers 334. FIG. 32D, and FIG. 31C
- 10 show the results after more pulses. Thread 324 has been thinned substantially. FIGS. 31D and 31E show the results after yet more pulses, which break up thread 324 and break graphite particles 338 into smaller and smaller fragments. After about 20 pulses, thread 324 has been completely broken up and most of the particles have been vaporized or broken into such small particles that they are almost invisible.
- 15 The tiny explosions of graphite thread 324 and of graphite particles 338 damage the dermal tissue within about 100 microns to 500 microns of thread 324. The greatest damage is closest to thread 324. For purposes of illustration, some damage is shown in the volume represented by circle 340 in FIG. 31F, lesser damage in the volume represented by circle 342 and still lesser damage in the volume represented by circle
- 20 344.

It is further believed that the above-described process creates a very thin, long wound within the dermis. Again, not wishing to be limited by any particular scientific or medical theory, it is believed that the beneficial results of the invention can probably be explained as follows. As with a normal skin wound, healing takes place over a

25 period of about 42 days. However, since the epidermis is not affected, the wound is largely not apparent and no surface scar is created, although there may be some slight swelling and redness. At the time of the injury, inflammatory chemicals are released, causing local blood vessels to dilate and become more permeable. Fluid, white blood cells, and blood proteins can then enter the wound site. At first, broken blood vessels

30 are plugged with clotted blood. However, within 2 to 5 days capillary buds invade the

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clots, restoring vascular supply. Fibroblasts enter the region and secrete collagen. Macrophages dispose of dead cells and other debris including small pieces of damaged collagen fibers. Over the next 40 days healing continues with new connective tissue gradually forming and creating strings of new fibers along the path of the

5 wound. The treated area should be prevented from undue stretching during the 40 day healing period. This allows new collagen fibers and associated elastin fibers to fully develop before too much stress is placed on them. The new tissue, like typical scar tissue, tends to shrink. This applies new tension to the treated skin sections. The new tension provides natural support to sagging skin with no scars and without any

10 unnatural appearance, such as may result from surgical face lift procedures.

Example 13 – Breast Lift Procedure

A breast lift procedure may be carried out similar to that described above with reference to a face lift procedure. Referring now to FIGS. 33A and 33B, a breast 346 is shown with grid lines 348 in a pattern under which graphite threads 324 are to be

15 implanted in the dermis. The illumination is as described above in the facial skin tightening process. As with that process, it is believed that long thin wounds are created in the dermis which are about 1 millimeter wide. It is recommended that a woman having this procedure wear a support bra for about 40 days following the breast lift procedure to prevent the breast skin from stretching too much during the

20 healing. As with the facelift, this is believed to allow new collagen fibers and associated elastin fibers to fully develop before too much stress is placed on the new fibers. The new tissue, like typical scar tissue, tends to shrink the treated skin sections, applying new tension to the skin that helps to lift the breasts.

Example 14 – Skin Tightening Procedure Using Particles

25 As an alternative to using graphite threads for a skin tightening procedure, small graphite particles can be implanted in selected patterns within the dermis by employing tattooing techniques. Any of the many well known tattoo techniques can be used to create the tattoo. Most of these well known procedures use an array of needles to

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punch a large number of small shallow holes in the skin into which the tattoo ink is rubbed. To be effective as a permanent tattoo, the ink has to be placed below the epidermis into the dermis.

In a skin tightening procedure, a tattoo-type solution to which 1 micron graphite particles have been added is used to create a pattern as shown in FIGS. 30A and 30C or in FIGS. 33A and 33B using conventional tattooing techniques. The graphite particles are deposited within the dermis in lines about 1 millimeter wide with a concentration of about 1,000 particles per millimeter of length. Illumination is the same as described above. The results are similar to using thread as described above.

- 10 A number of embodiments of the present invention have been described. Nevertheless, it will be understood that various modifications may be made without departing from the spirit and scope of the invention. Accordingly, other embodiments are within the scope of the following claims.

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WHAT IS CLAIMED IS:

1. A method of bleaching hair growing from hair ducts located in a section of skin, the hairs including melanosomes, the method including:
 - 5 (a) applying to the section of skin a fluid that is transparent to light at or near at least one frequency absorbed by melanosomes and that has an index of refraction that is greater than the index of refraction of the skin, the applying including causing a portion of the fluid to enter hair ducts in the section of skin;
 - 10 (b) illuminating a region of the section of skin with light at the at least one frequency, including directing the illuminating light so that a portion thereof is conducted through the fluid in hair ducts located in the region of the section of skin, and a remaining portion of the illuminating light impinges on a surface of the region of the section of skin or impinges on hairs located above the surface, at least some of the illuminating light being absorbed by
15 melanosomes in the hairs, the illuminating being of an fluence and duration to cause destruction or otherwise causing damage to enough of the melanosomes in the hair to bleach hair both above and below the surface of the skin without causing significant damage to surrounding skin tissue.

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2. A method of destroying papillae located in hair ducts located in a section of skin, the papillae including melanosomes, the method including:
- (a) applying to the section of skin a fluid that is transparent to light at or near at least one wavelength absorbed by the melanosomes and that has an index of refraction that is greater than that of skin tissue, including causing a portion of said fluid to enter hair ducts in the section of skin;
- (b) illuminating a region of the section of skin with pulses of light at the at least one wavelength, including directing the illuminating light so that a portion thereof is conducted through the fluid to papillae in hair ducts located in the region of the section of skin, wherein another portion of the illuminating light is transmitted through the skin to the papillae in the hair ducts located in the region of the section of skin, at least some of the illuminating light being absorbed by the melanosomes in the illuminated papillae and causing heating of the illuminated papillae to a temperature of about 30-90 degrees Celsius above ambient skin temperature with each pulse without vaporizing the melanosomes in the papillae;
- (c) inhibiting generalized damage to skin tissue in the region of the section of skin, including cooling the region of the section of skin.

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3. A method of inhibiting growth of hair from papillae located at the bottoms of hair ducts in a section of skin, including:
- (a) removing hairs from the hair ducts in the section of skin;
 - (b) applying a contaminant to the section of skin, the contaminant having a high
5 absorption at or near at least one frequency band of light;
 - (c) causing at least a portion of the contaminant to move to the bottoms of the ducts from which the hair has been removed;
 - (d) filling the hair ducts with a light guide medium having an index of refraction that is greater than that of skin tissue; and
 - 10 (e) illuminating a region of the section of skin with light at the at least one frequency band, including transmitting the illuminating light through the light guide medium in the hair ducts to the contaminant, the contaminant at the bottoms of the hair ducts absorbing energy from the illuminating light and transmitting at least a portion of the absorbed energy to the papillae at the
15 bottoms of the hair ducts, thereby damaging the papillae with the transmitted energy.
4. A method of transdermal drug delivery, including:
- (a) removing about 10 to 20 layers of stratum corneum cells from a section of a
20 patient's skin without significantly damaging underlying layers of epithelium cells, including applying laser light to the section of skin; and
 - (b) applying a drug to the section of skin.

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5. A method of electrically sensing a body function of a person, including:
 - (a) removing about 10 to 20 layers of stratum corneum cells from a section of a person's skin without significantly damaging underlying layers of epithelium cells, including applying laser light to the section of skin;
 - 5 (b) applying an electronic sensor to the section of skin; and
 - (c) sensing an electric signal produced by the patient with the sensor.
6. A method of imaging subsurface tissue structures, including:
 - (a) scanning pulses of light in a focal plane below a surface a tissue, including producing a reflected signal from the tissue;
 - 10 (b) time gating the reflected signal to eliminate a portion of the reflected signal outside a selected time period; and
 - (c) imaging the time gated reflected signal with a confocal microscope sensor.
7. A method of delivering a drug or active substance to a person, including:
 - (a) applying a composition to a section of skin of the person, the composition
15 including a drug or active substance bound to biodegradable carriers, the section of skin including hair ducts;
 - (b) causing the composition to enter the hair ducts; and
 - (c) permitting the drug or active substance to be released in the hair ducts as the carriers degrade over a period of time.

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8. An apparatus for cooling a section of skin being illuminated with laser light, including:
- (a) a window that is transparent to the light; and
 - (b) a support for the window, including:
- 5 (c) a member fabricated of a material with a high thermal conductivity, the member having a central opening for the passage of the light, the window being held by the member at one end thereof, and the window being in good thermal contact with the member; and
- 10 (d) an active heat exchanger structured and arranged to remove heat from the member.
9. A skin treatment process for increasing the tension and elasticity in a region of human skin including dermal tissue, including the steps of:
- (a) placing in the dermis an energy absorbing material having a high optical absorption of at least one frequency band of light; and
- 15 (b) illuminating the region of skin with the at least one frequency band of light, a portion of which penetrates the region of skin and is absorbed in the energy absorbing material thereby affecting the dermal tissue to provide increased and elasticity for the skin region.
10. A process as in Claim 1, wherein said energy absorbing material comprises
- 20 graphite.

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11. A skin treatment system for increasing the tension and elasticity in a region of human skin including dermal tissue, including:
- (a) an energy absorbing material disposed in the region of skin and having a high optical absorption of at least one frequency band of light; and
 - 5 (b) light source spaced apart from the region of skin and being for illuminating the region of skin with the at least one frequency band of light, a portion of which penetrates the region of skin and is absorbed in the energy absorbing material thereby affecting the dermal tissue to provide increased tension and elasticity for the skin region.

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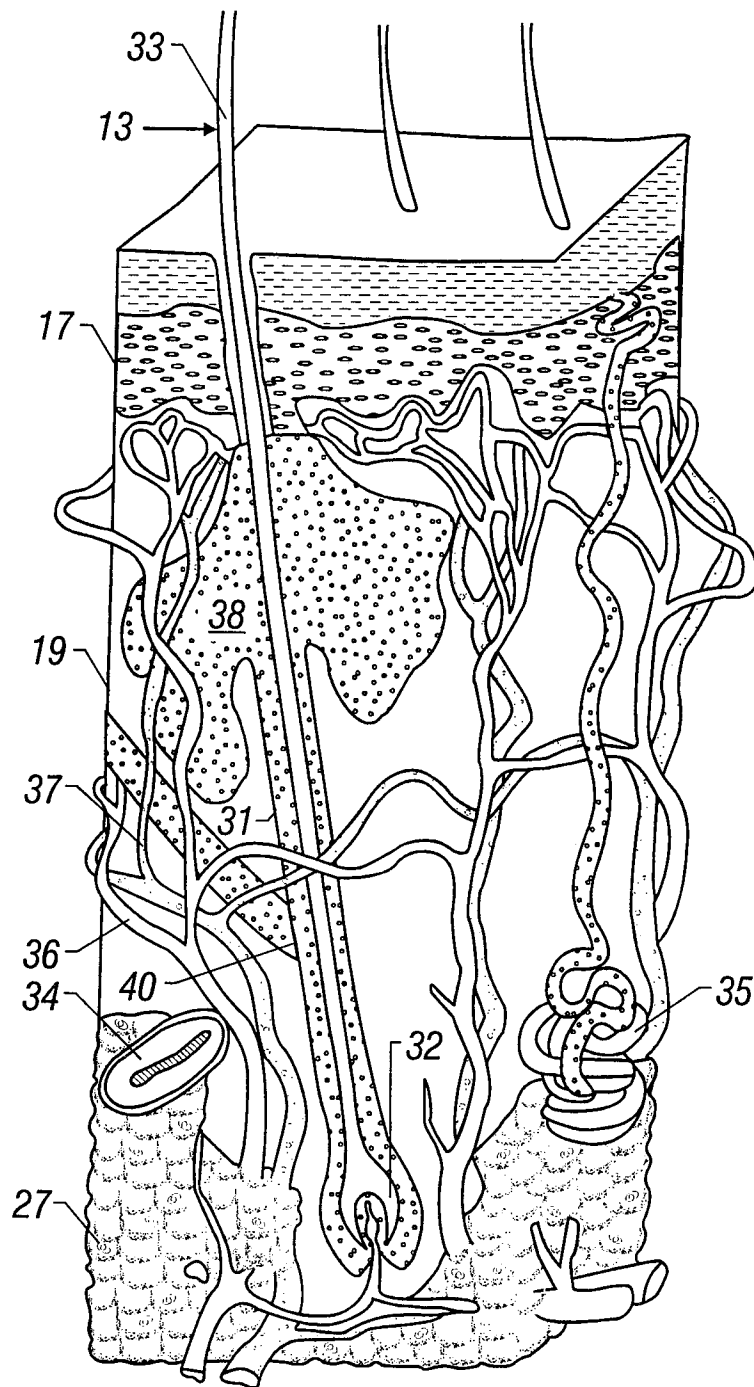


FIG. 1

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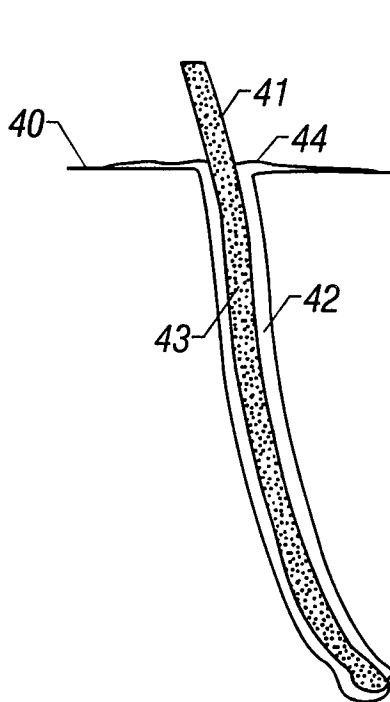


FIG. 2A

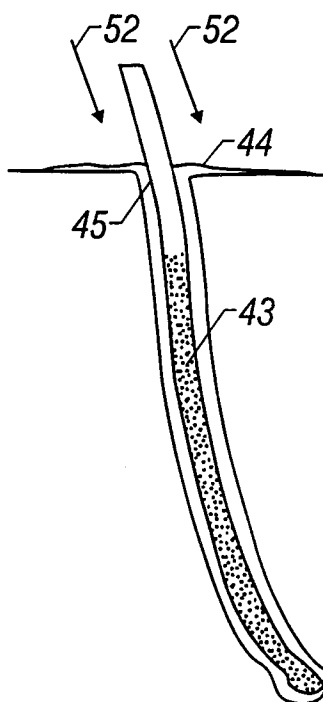


FIG. 2B

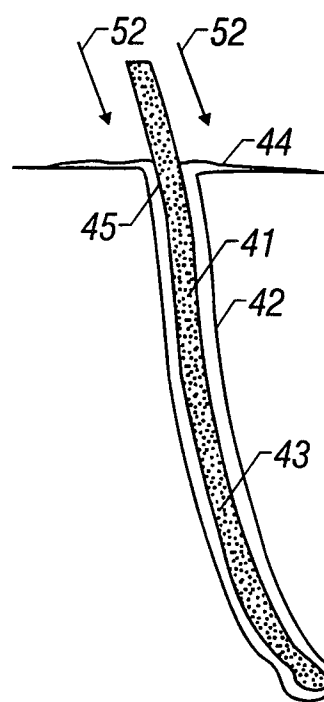


FIG. 2C

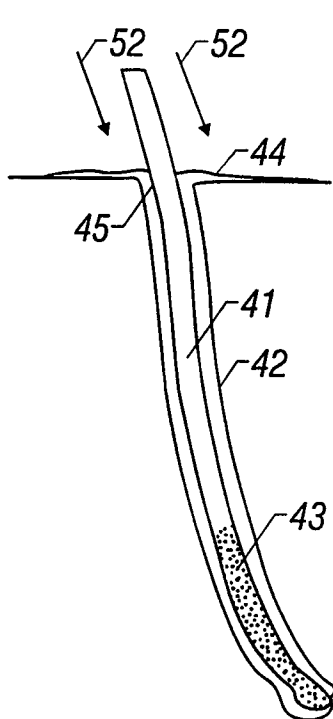


FIG. 2D

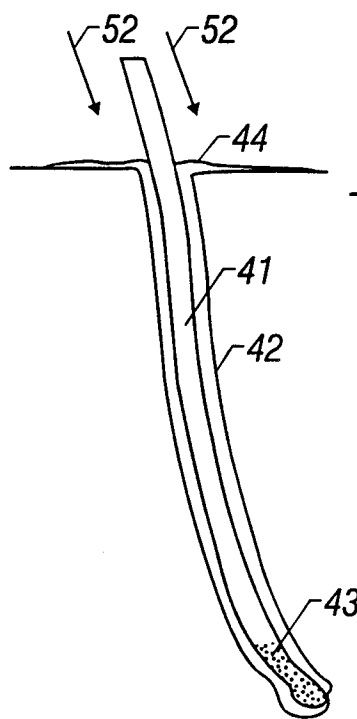


FIG. 2E

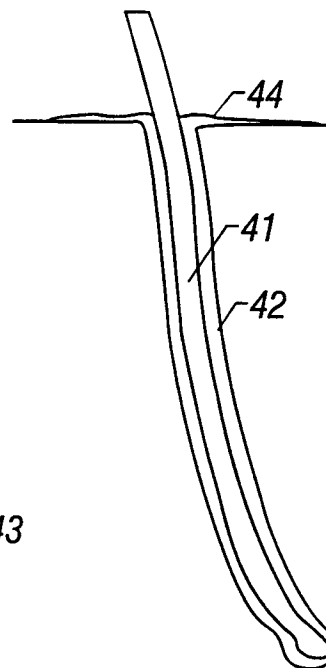


FIG. 2F

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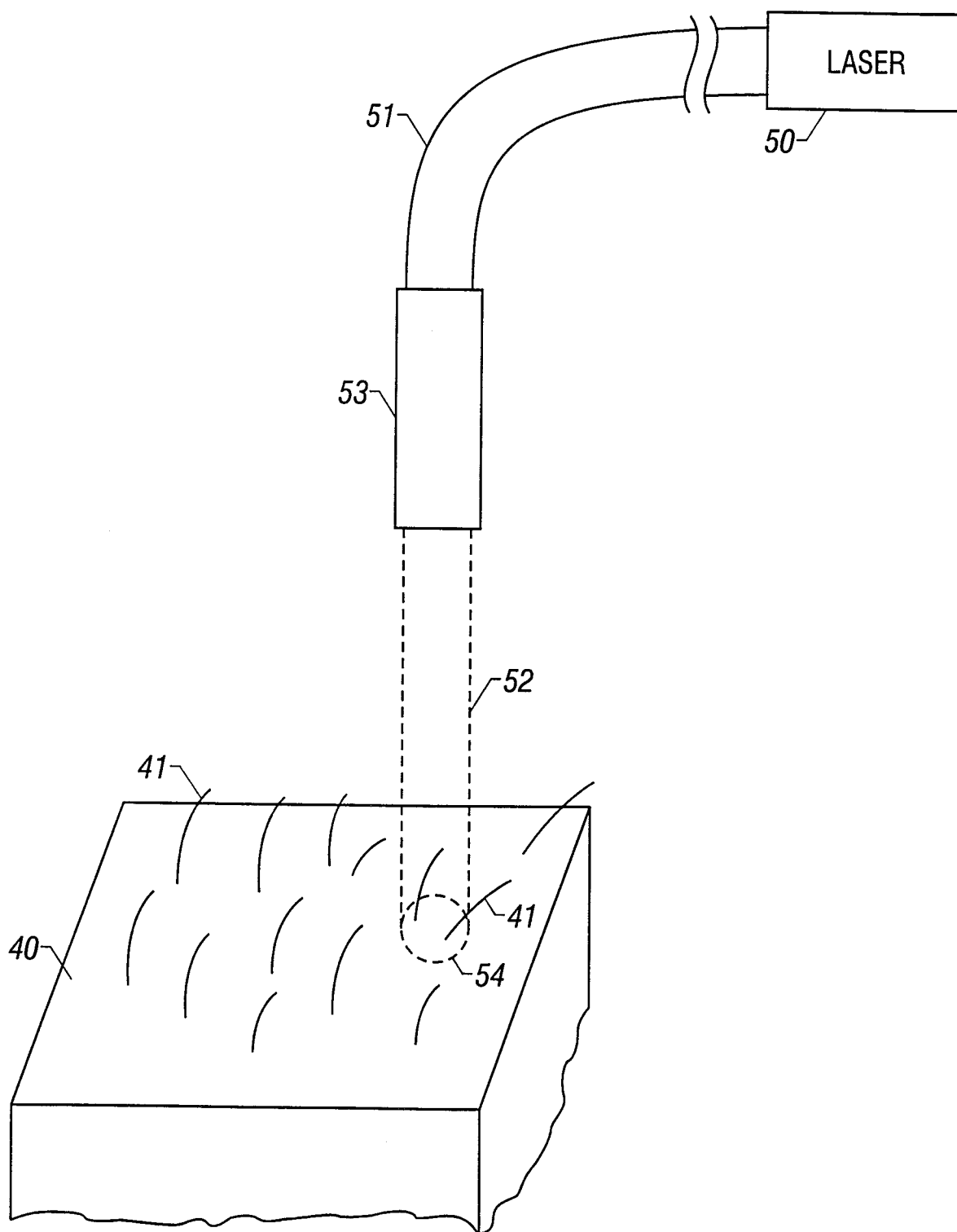


FIG. 3

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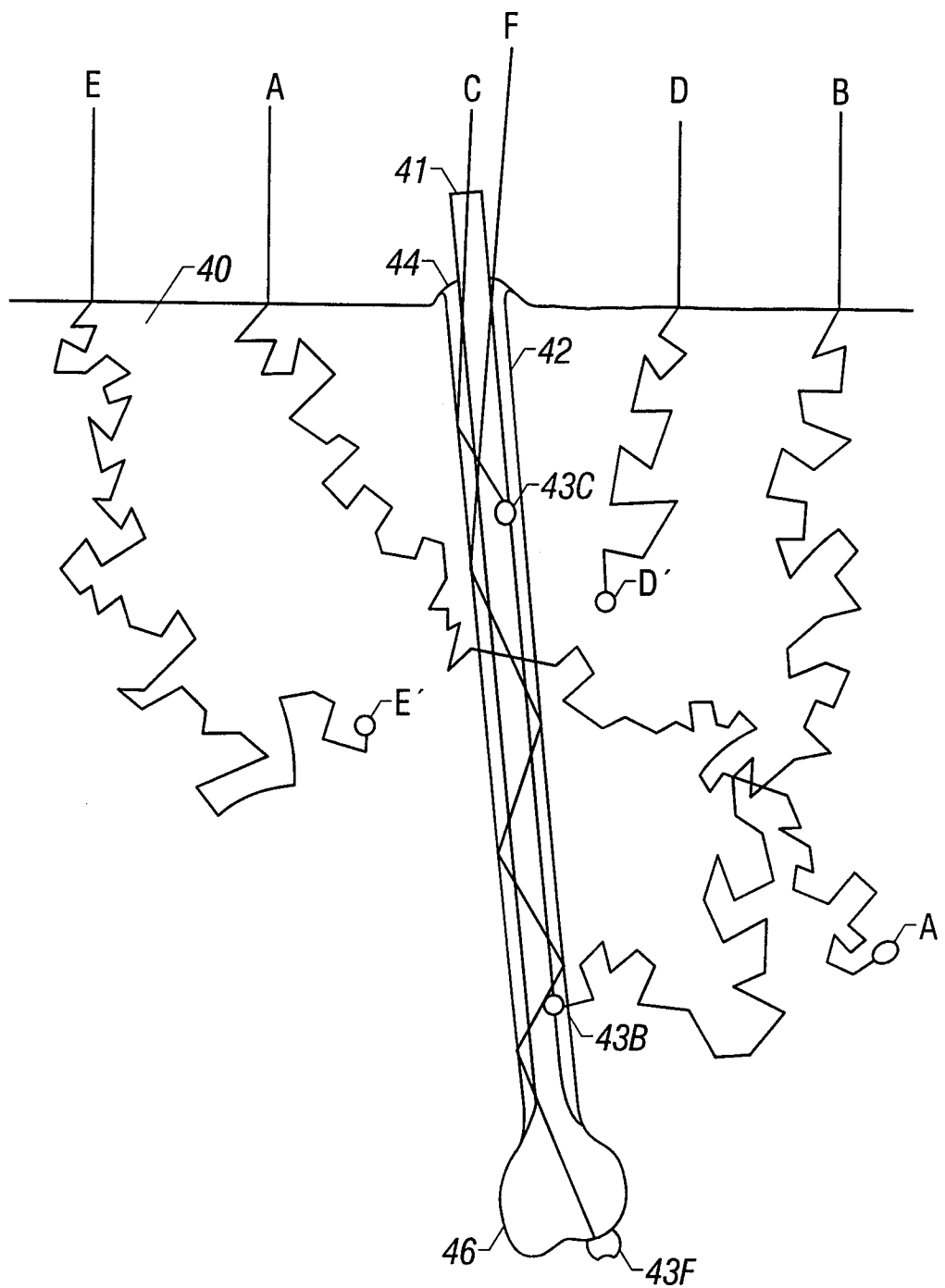


FIG. 4

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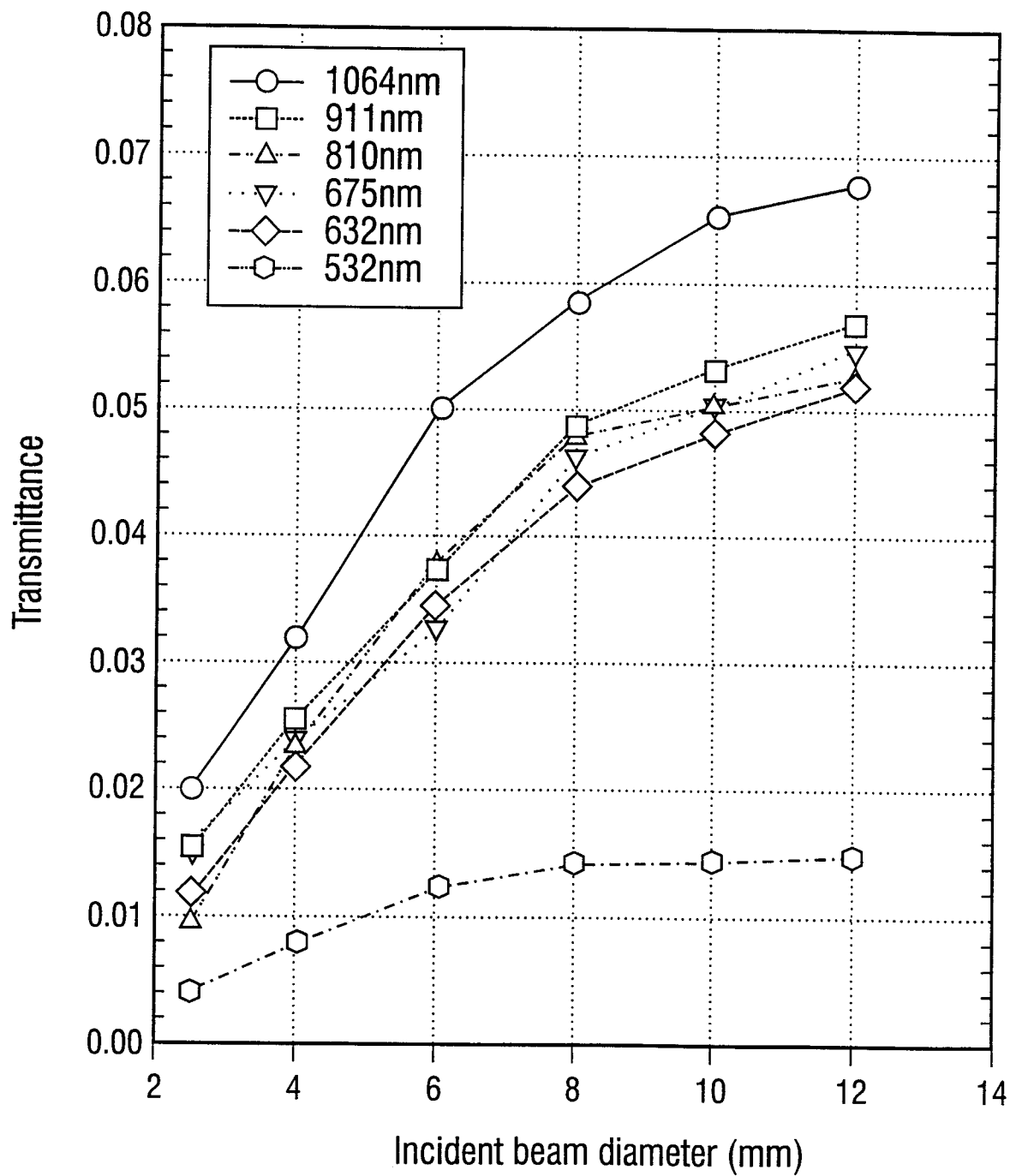
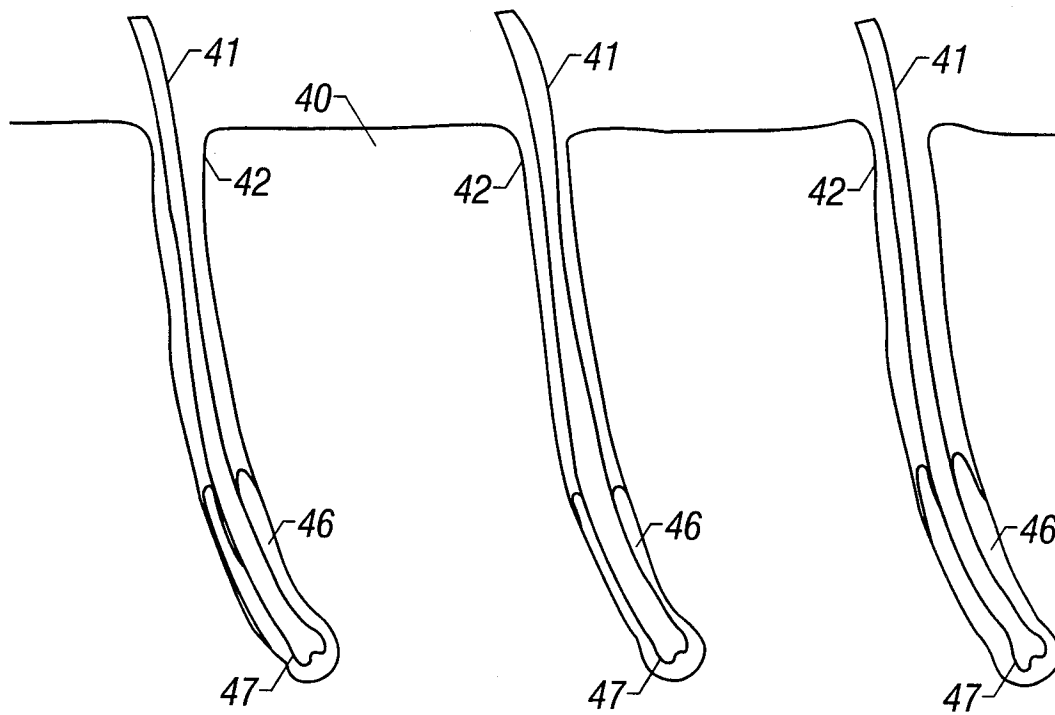


FIG. 5

6/36**FIG. 6**

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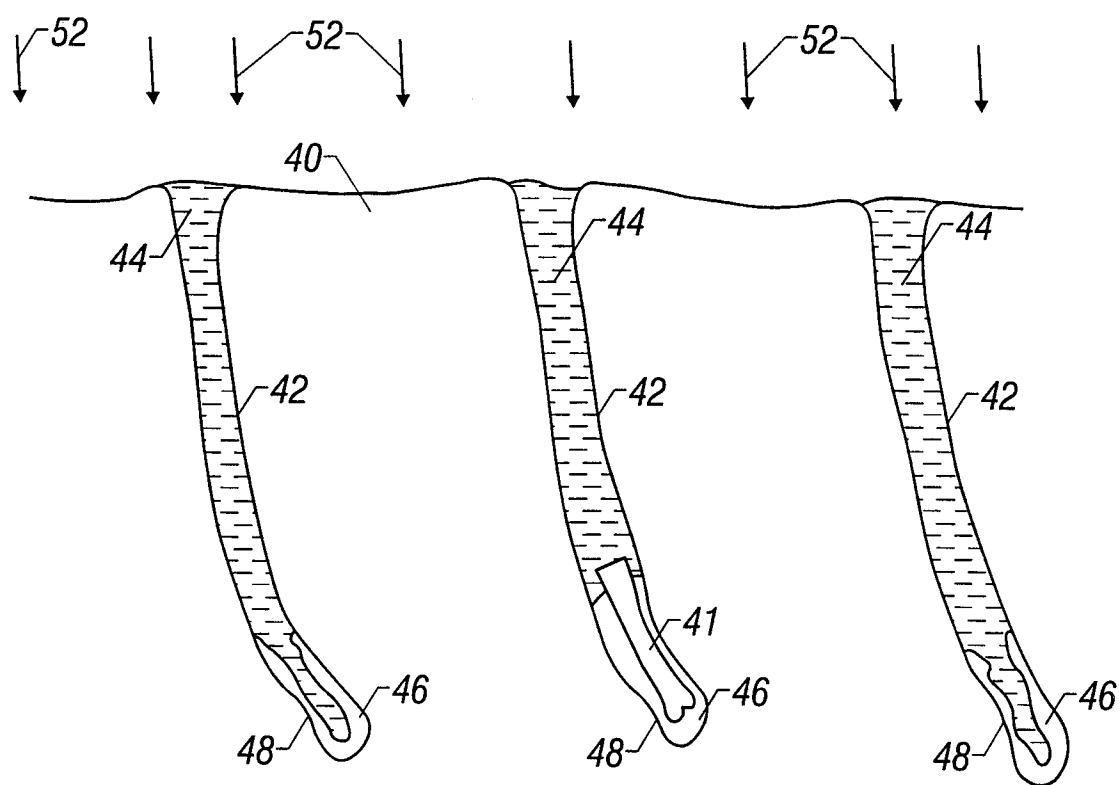


FIG. 7

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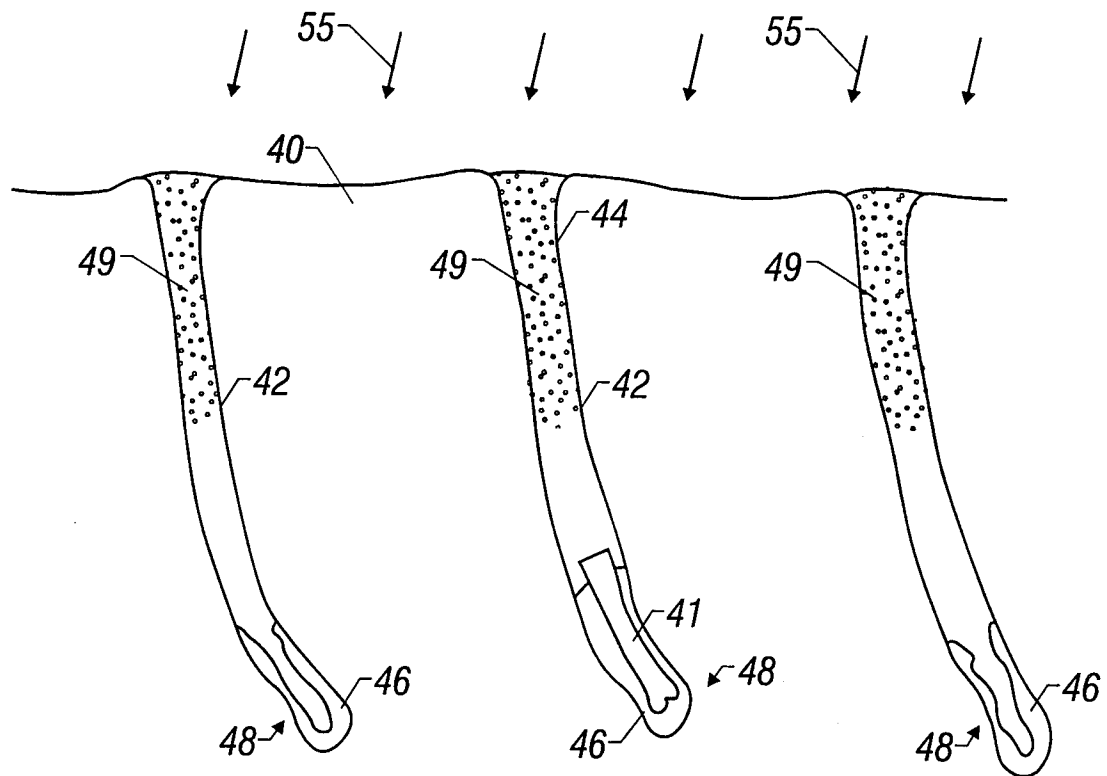


FIG. 8

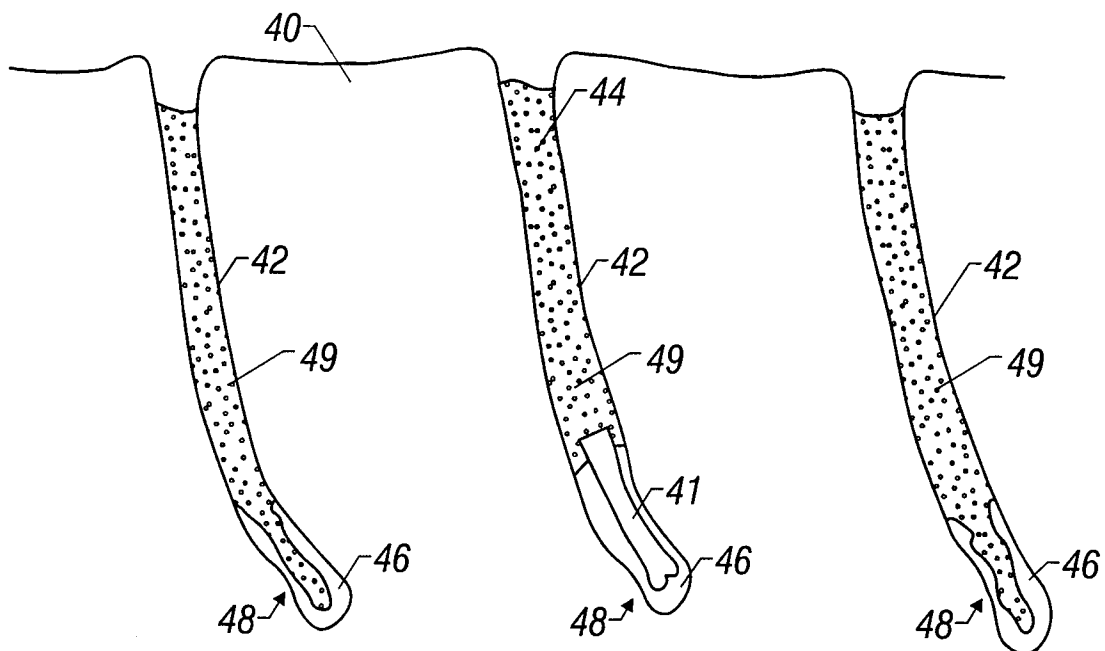


FIG. 9

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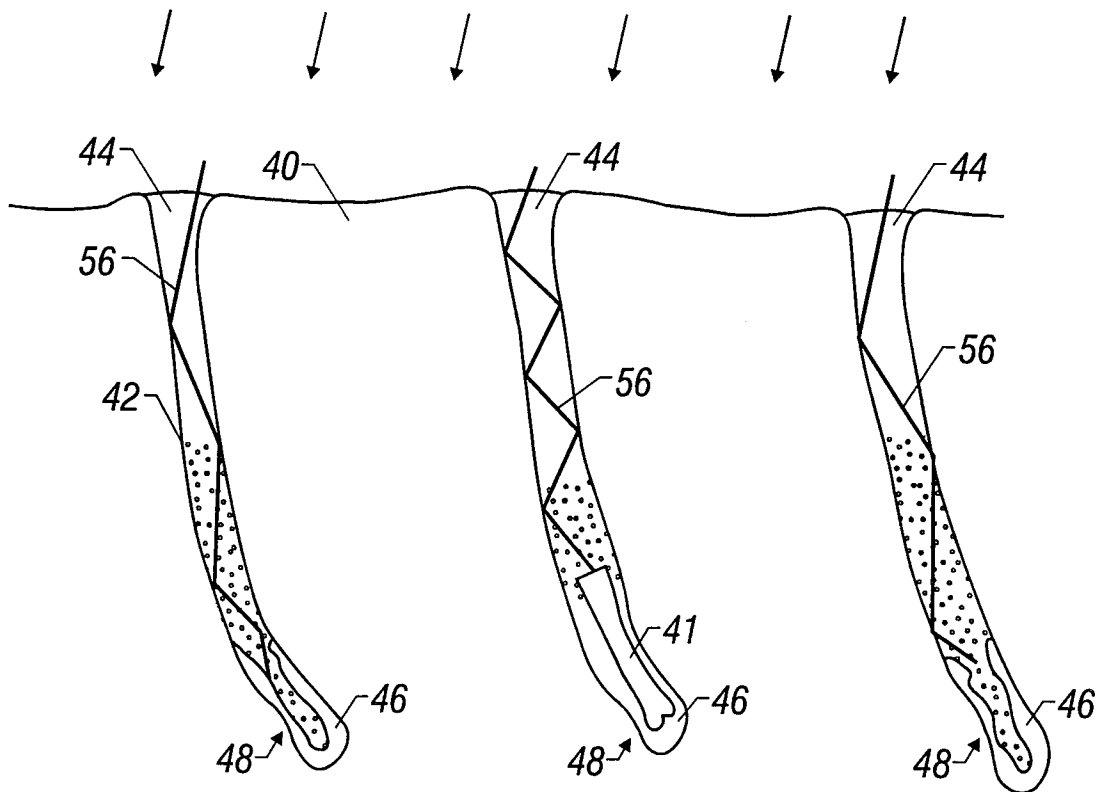
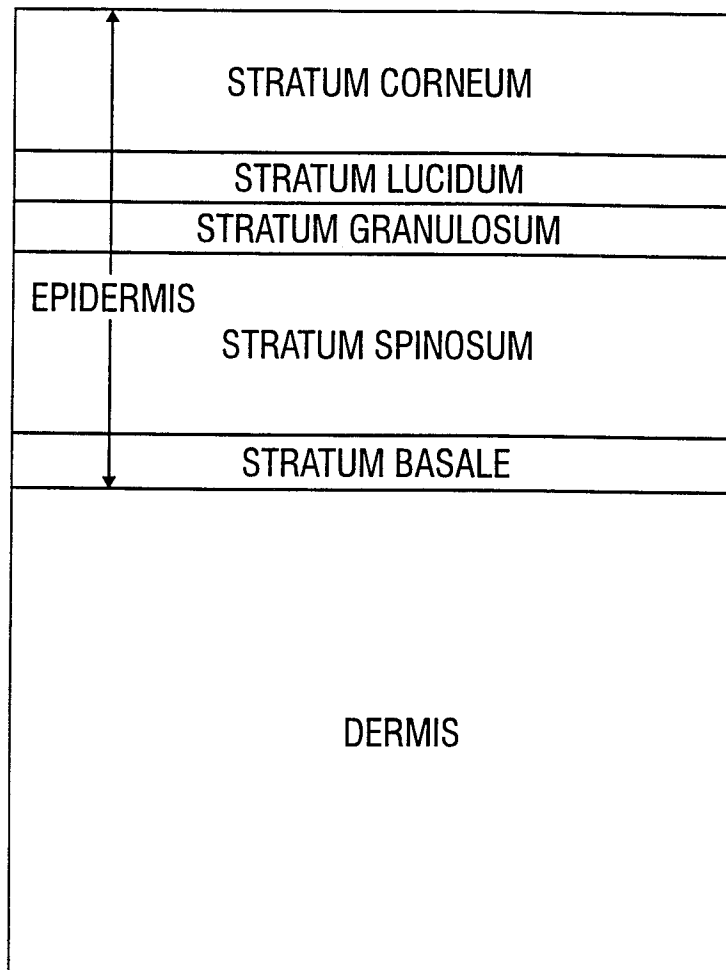
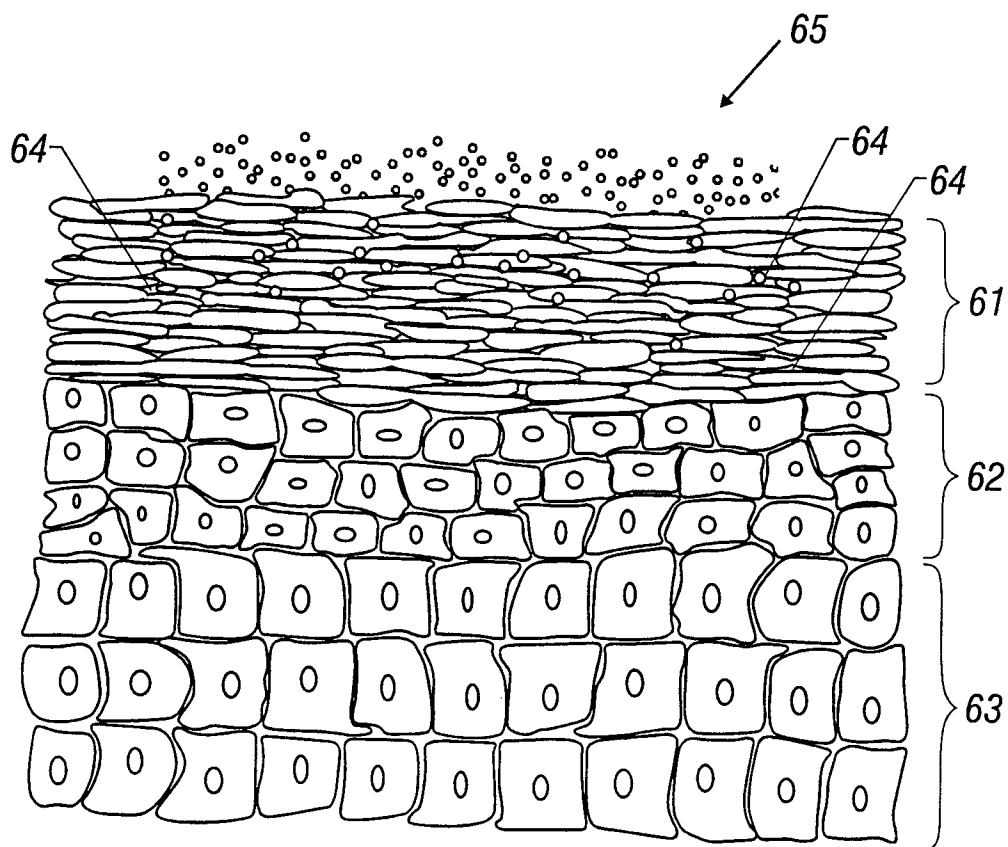


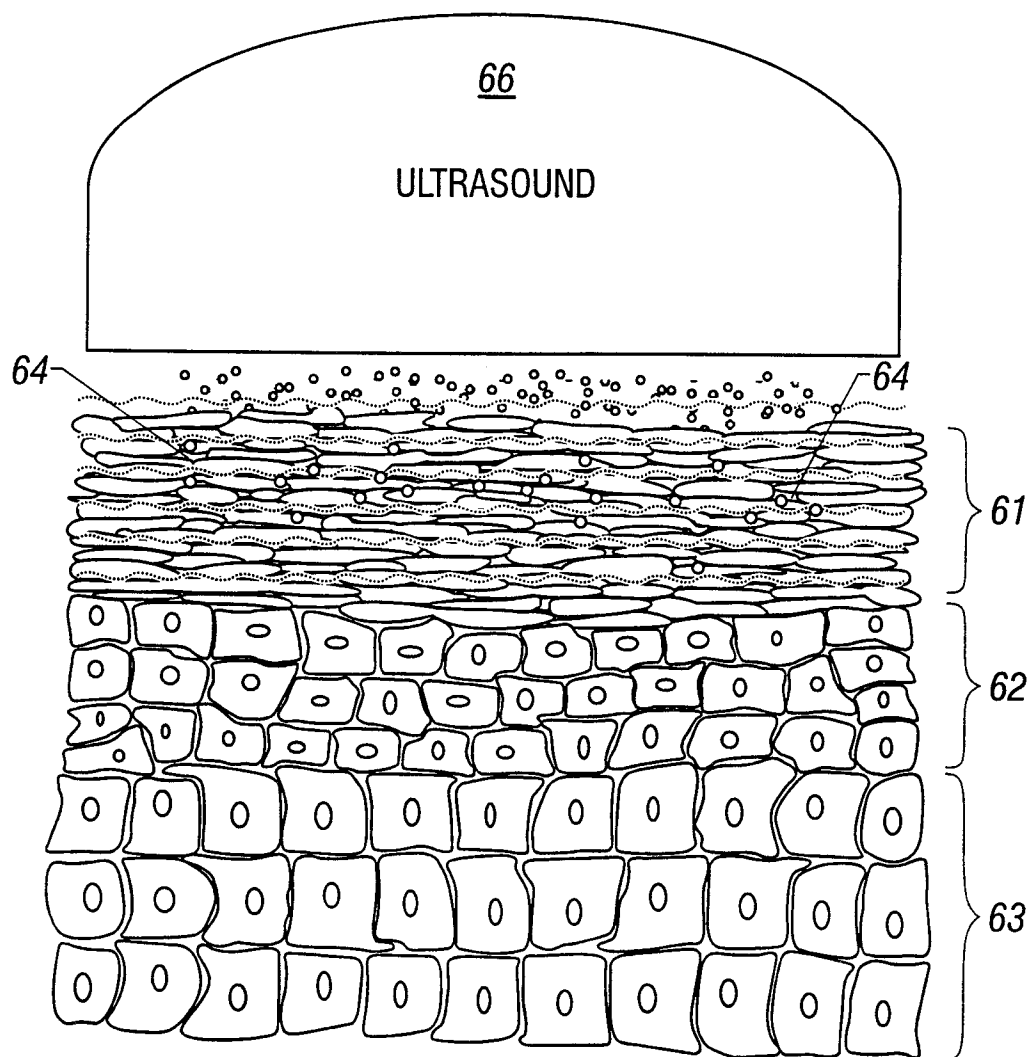
FIG. 10

10/36**FIG. 11**

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**FIG. 12**

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**FIG. 13**

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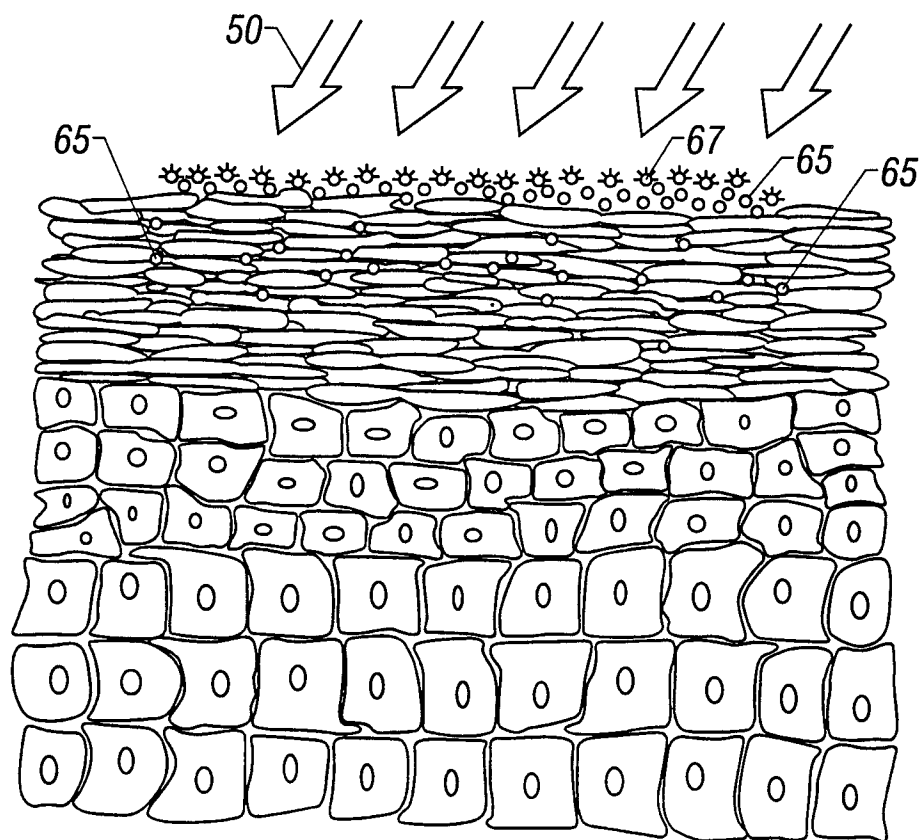


FIG. 14

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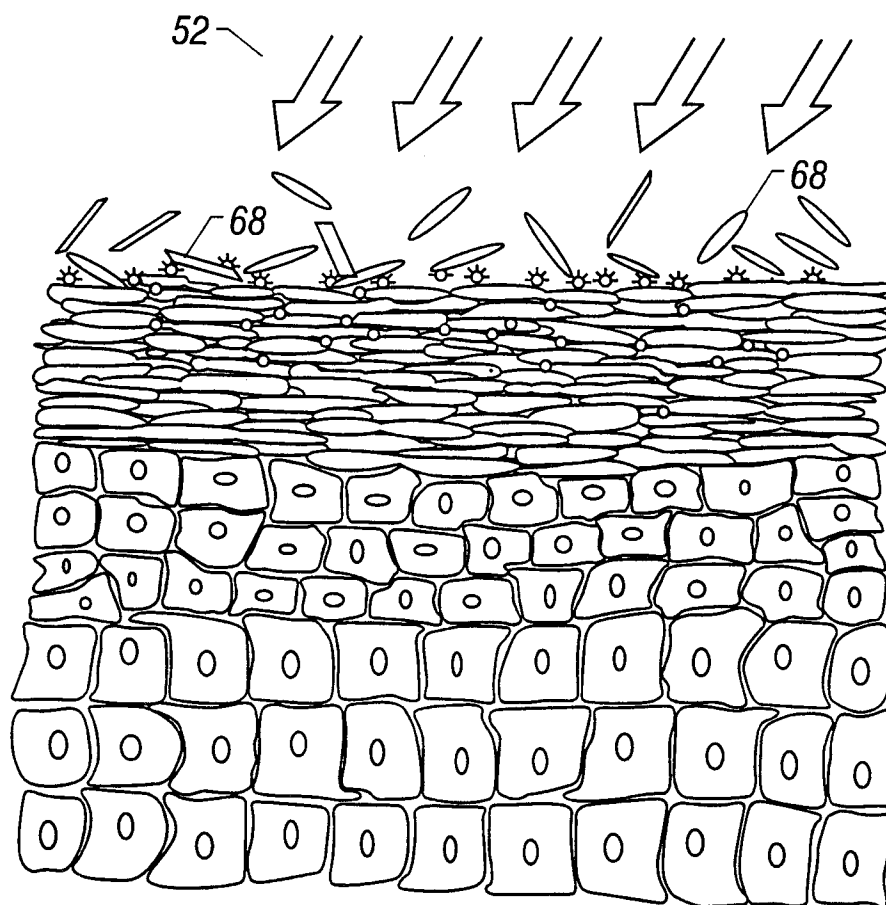
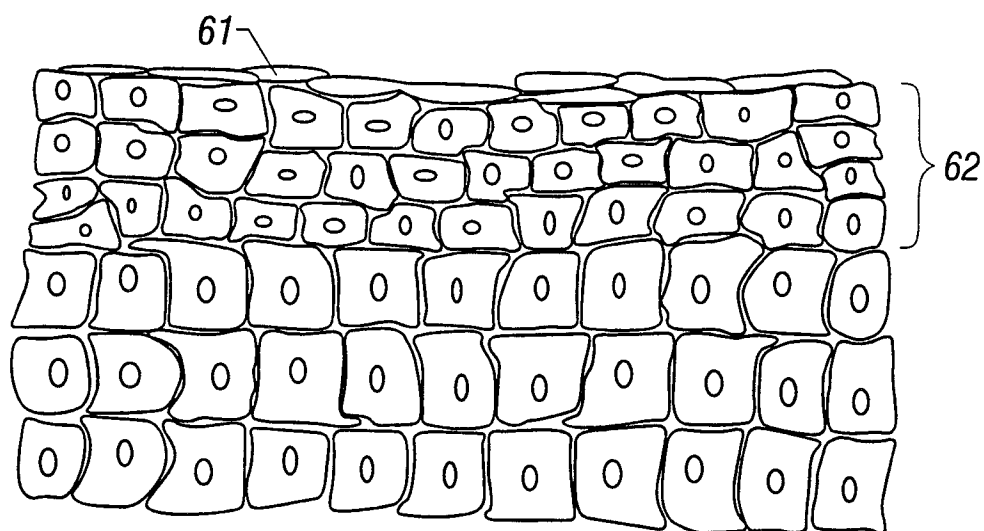
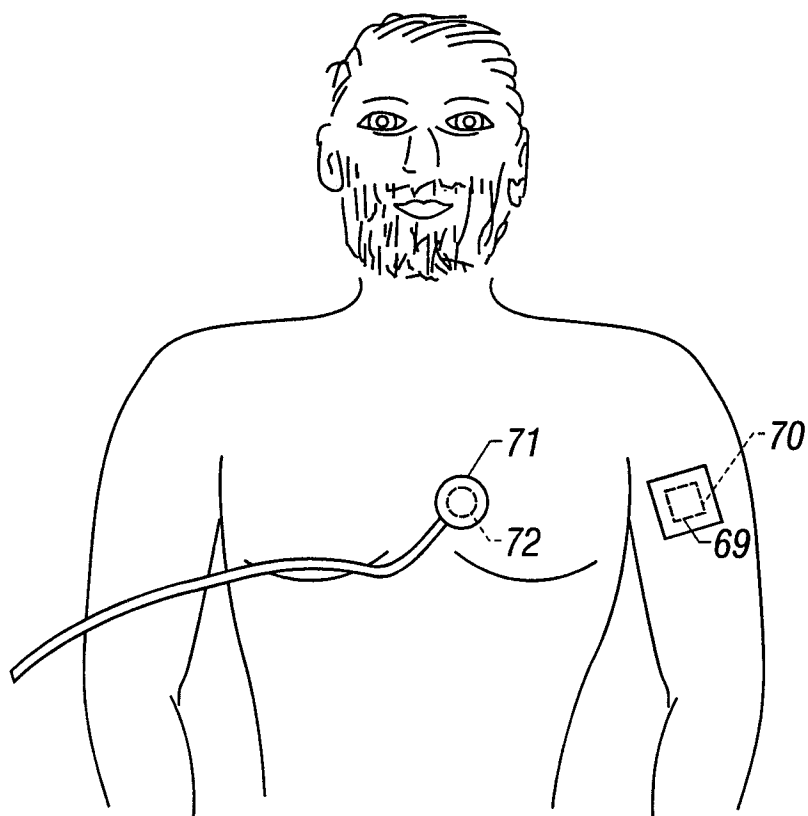


FIG. 15

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**FIG. 16**

16/36**FIG. 17**

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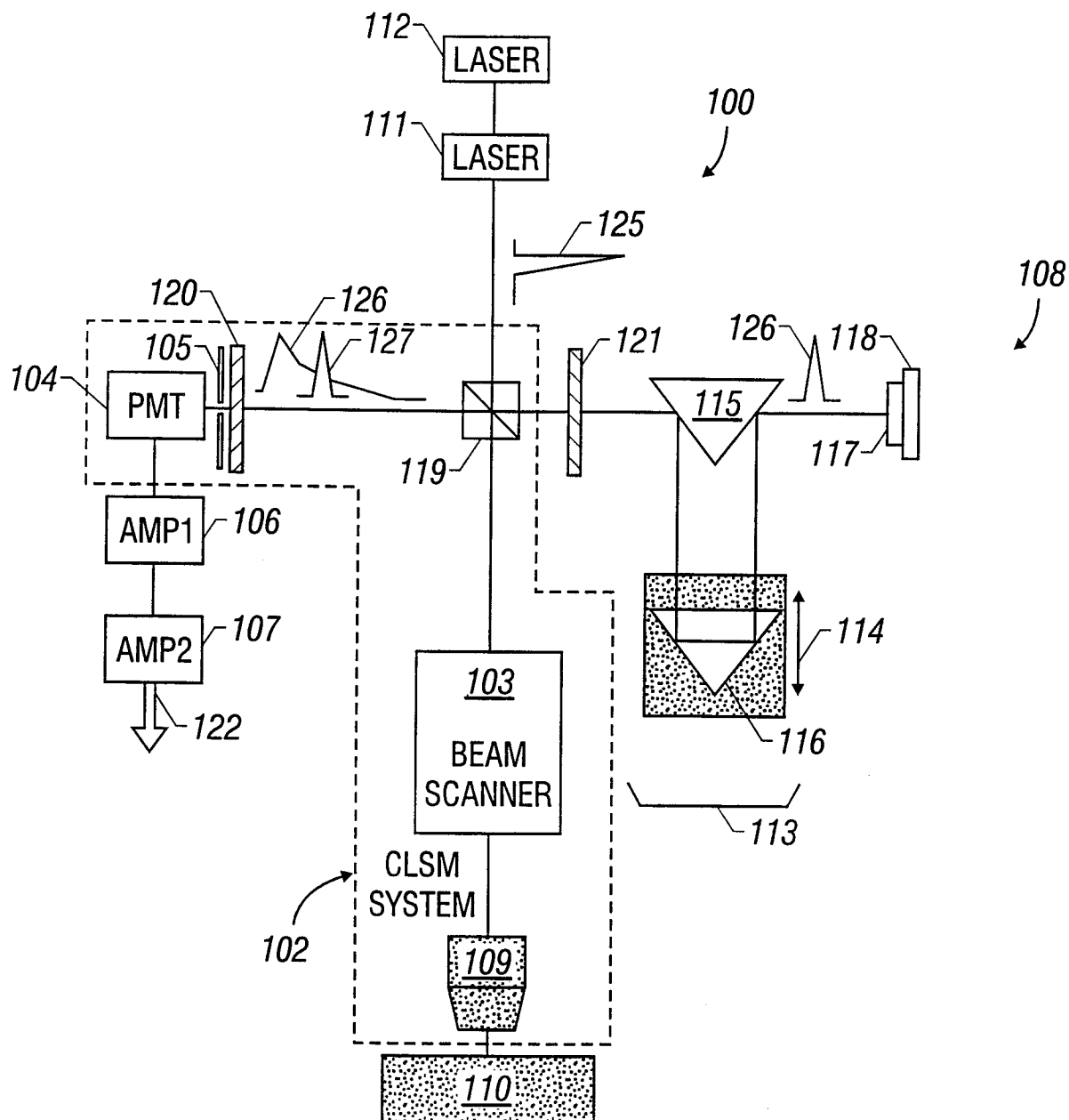
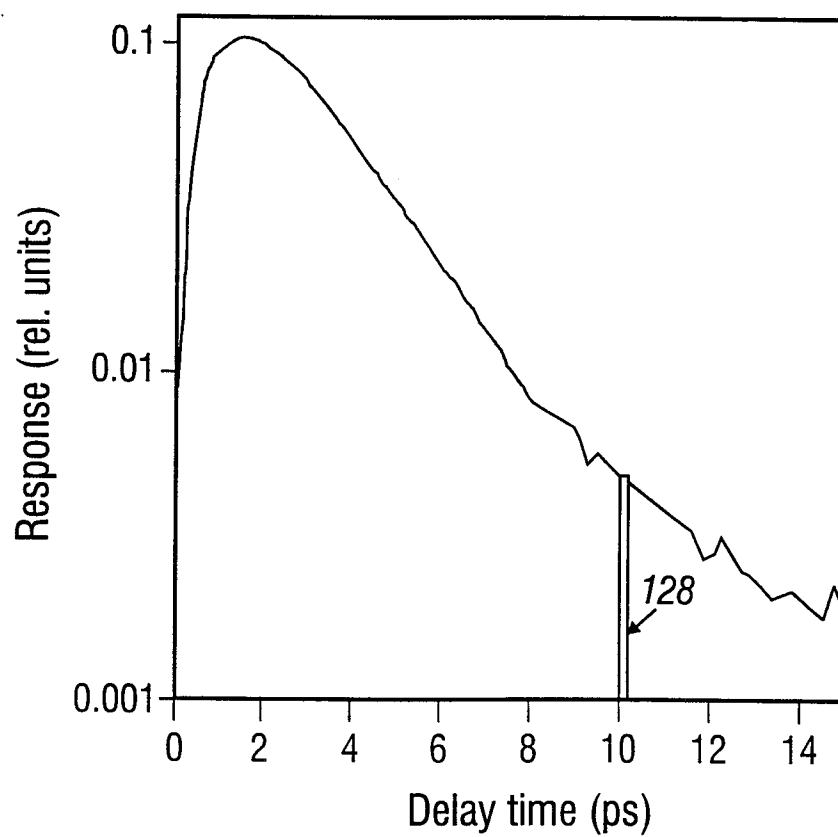


FIG. 18

18/36**FIG. 19**

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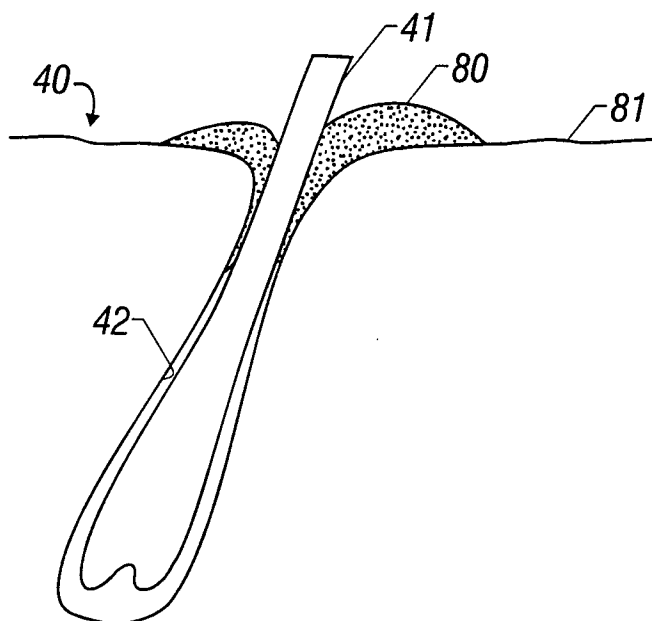


FIG. 20

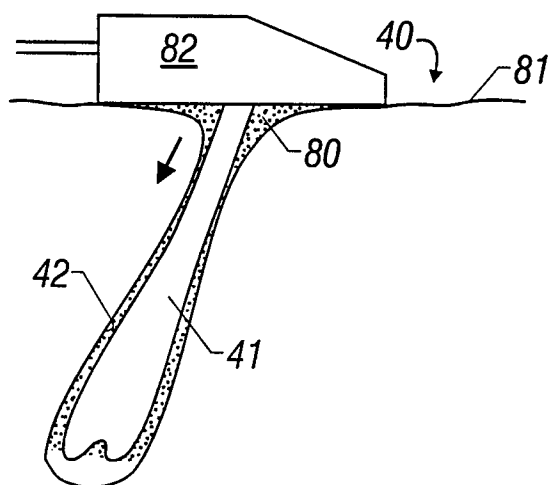
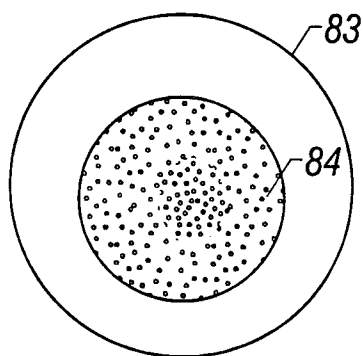
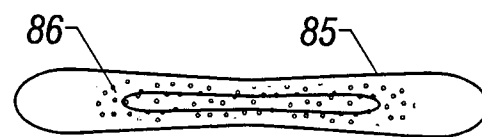
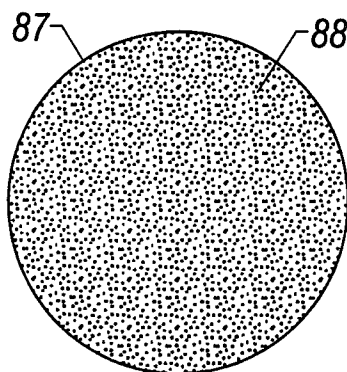
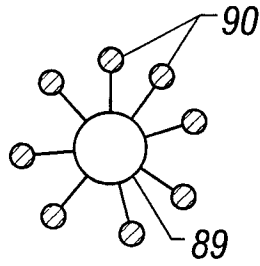
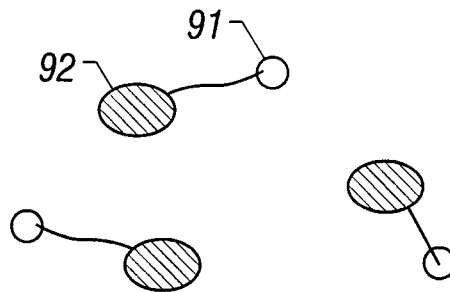


FIG. 21

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**FIG. 22A****FIG. 22B****FIG. 22C**

21/36**FIG. 22D****FIG. 22E**

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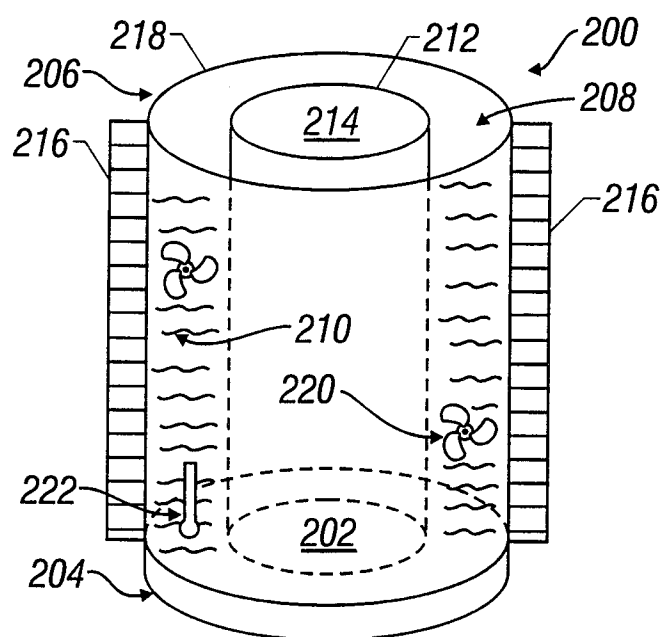
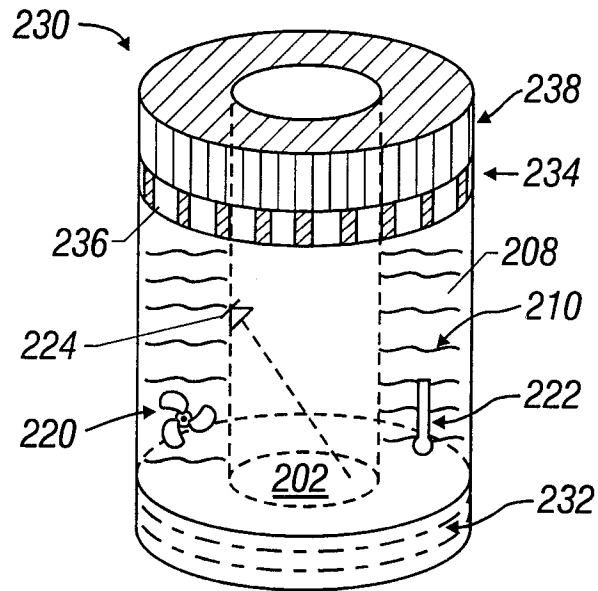
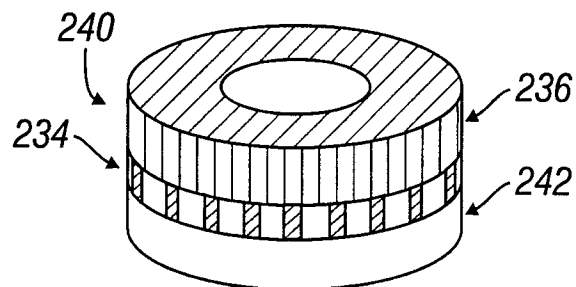


FIG. 23

23/36**FIG. 24****FIG. 25**

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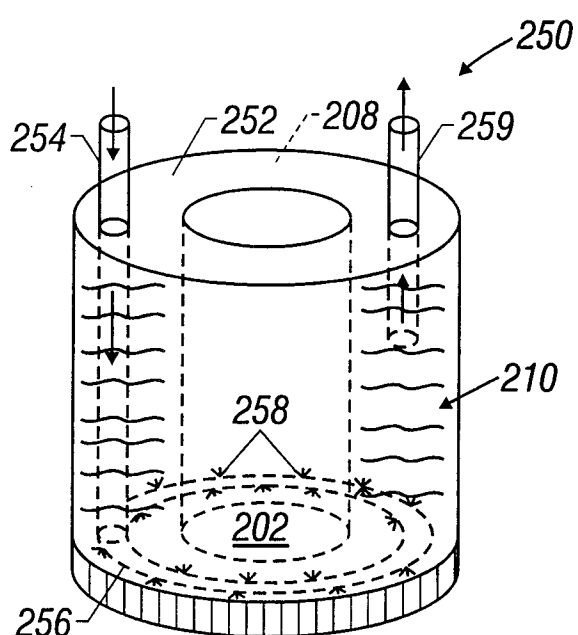


FIG. 26

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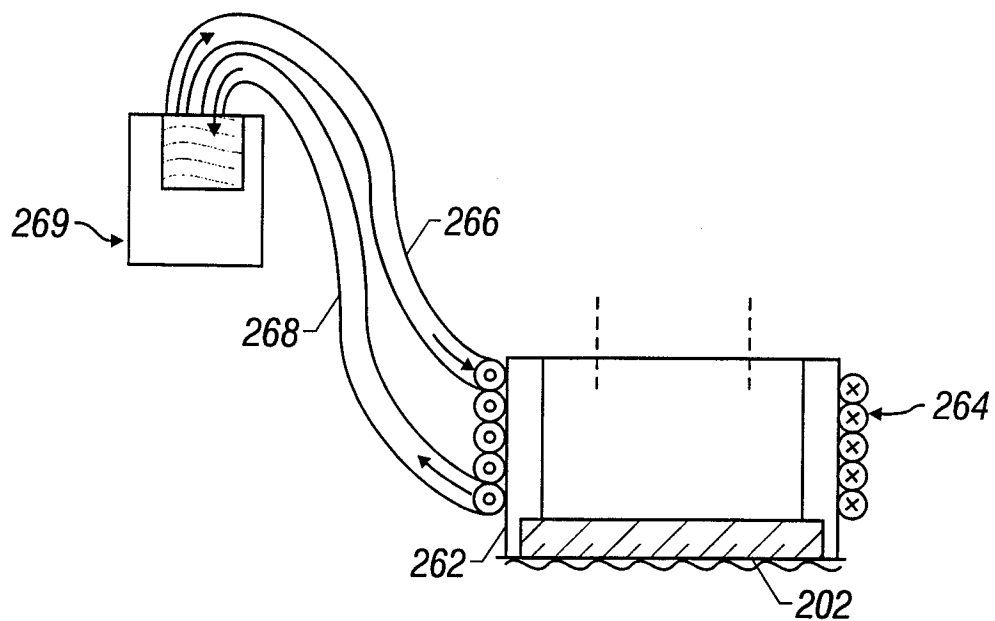


FIG. 27

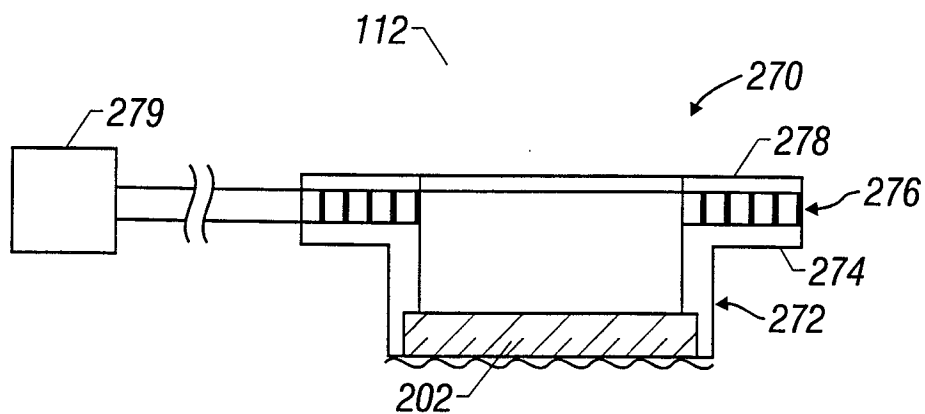


FIG. 28

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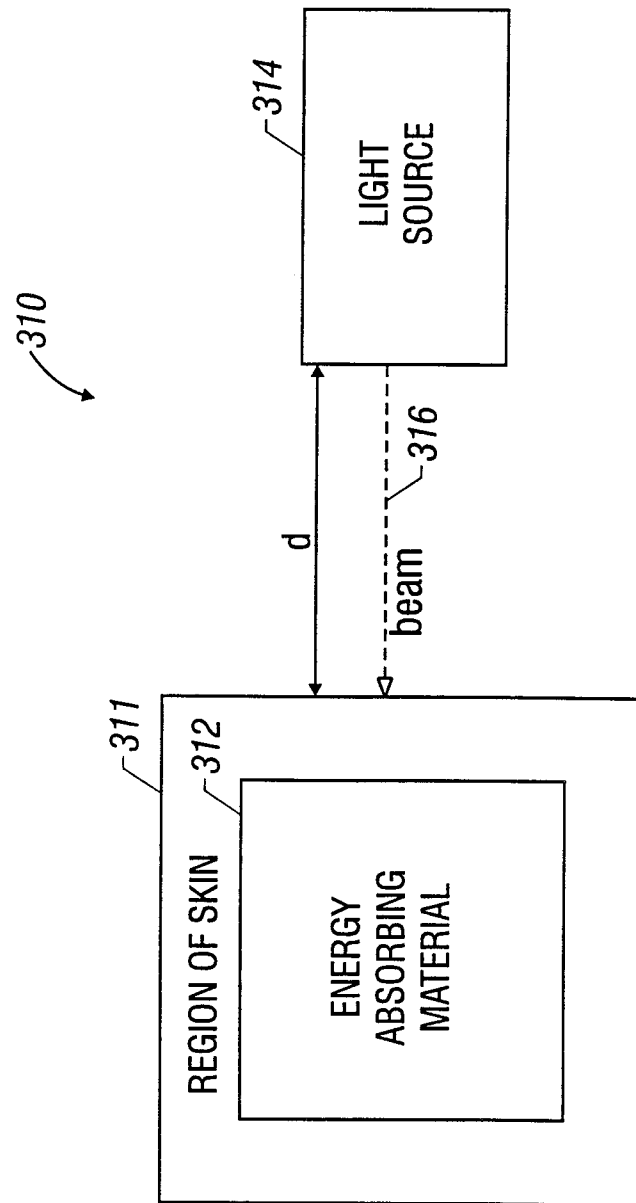


FIG. 29

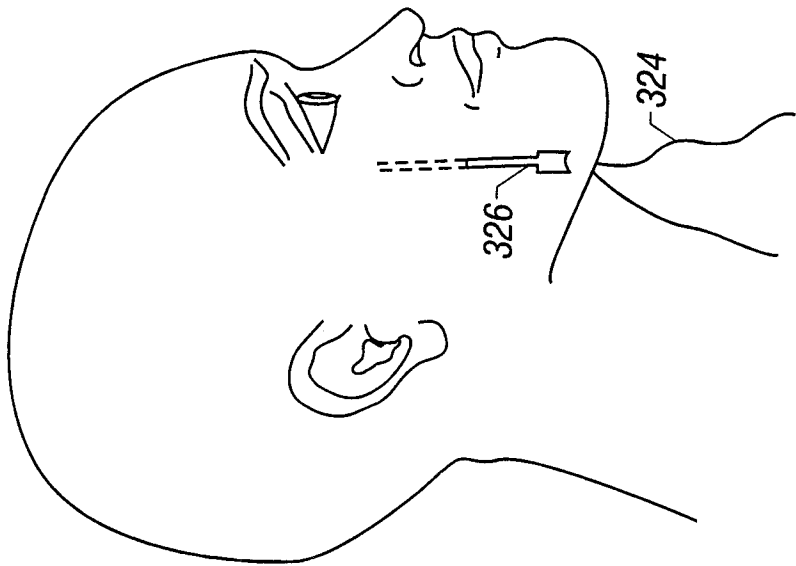


FIG. 30B

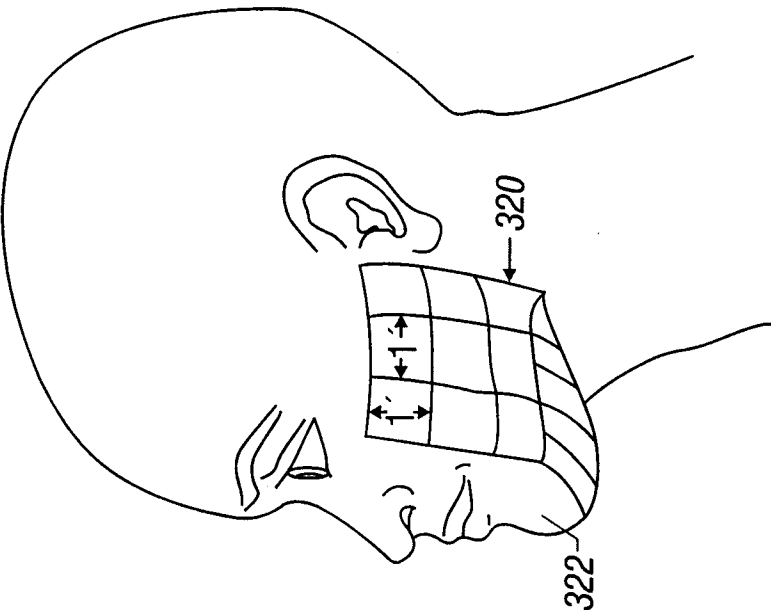


FIG. 30A

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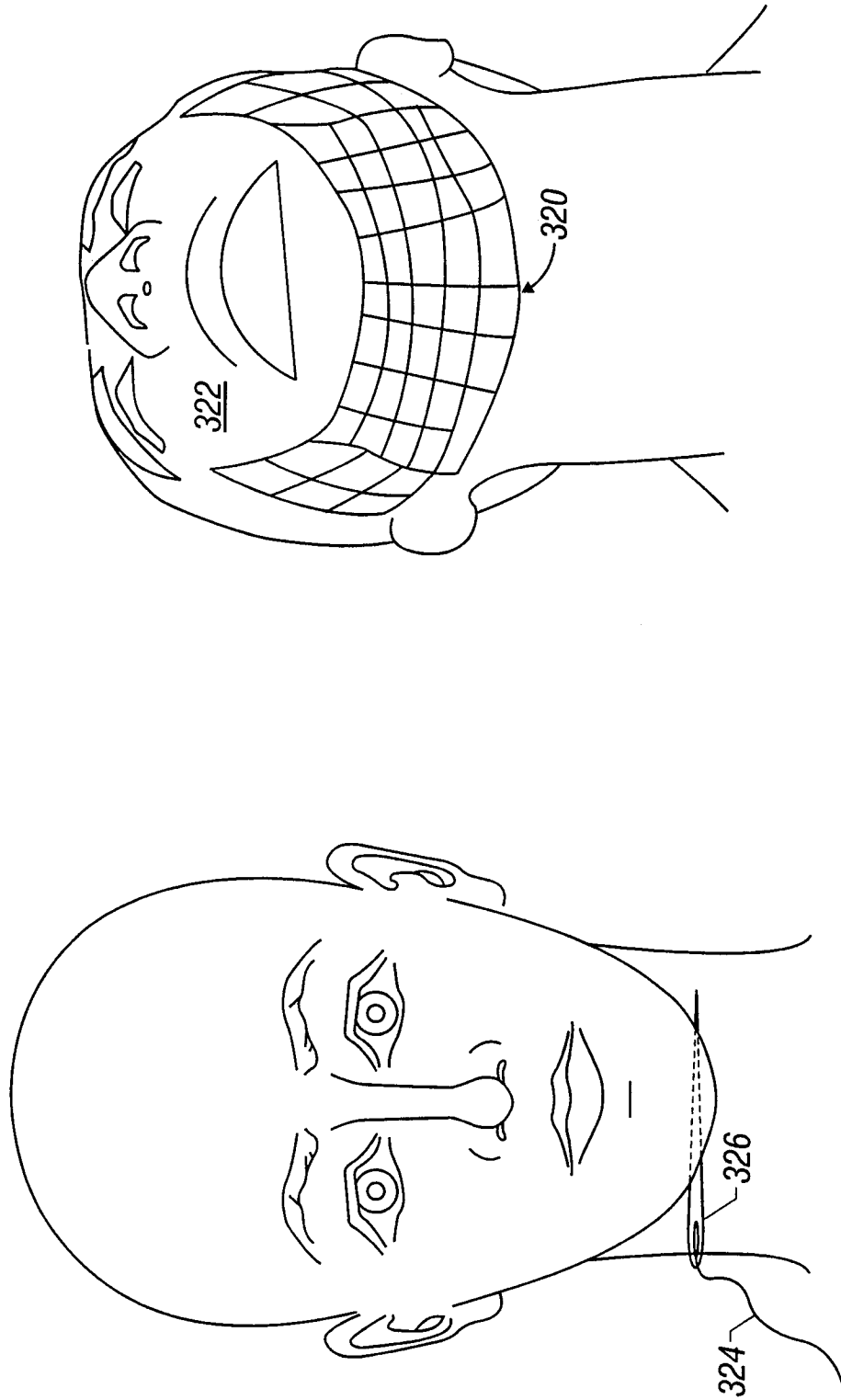


FIG. 30D

FIG. 30C

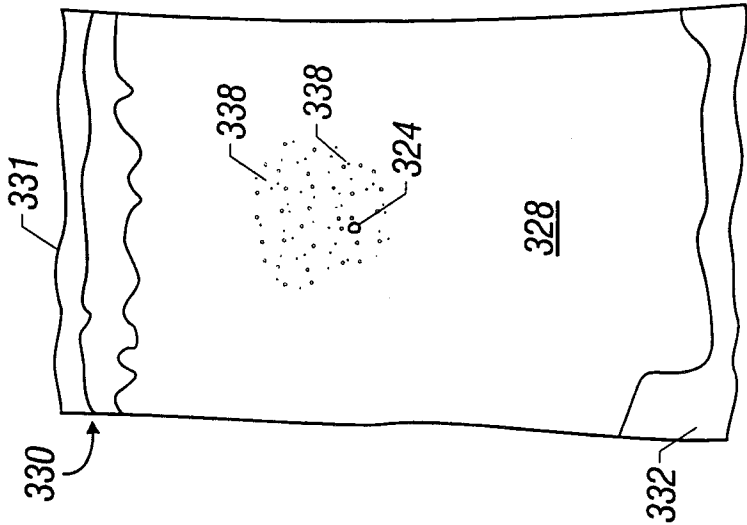


FIG. 31B

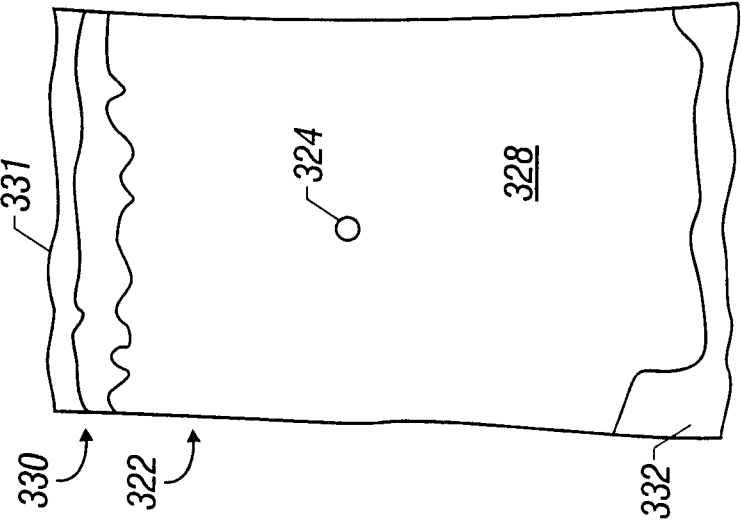


FIG. 31A

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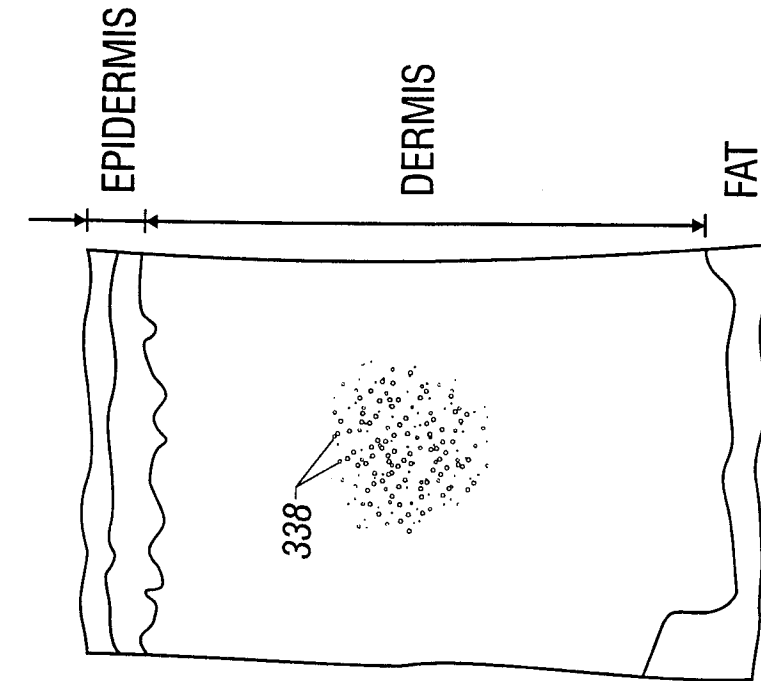


FIG. 31D

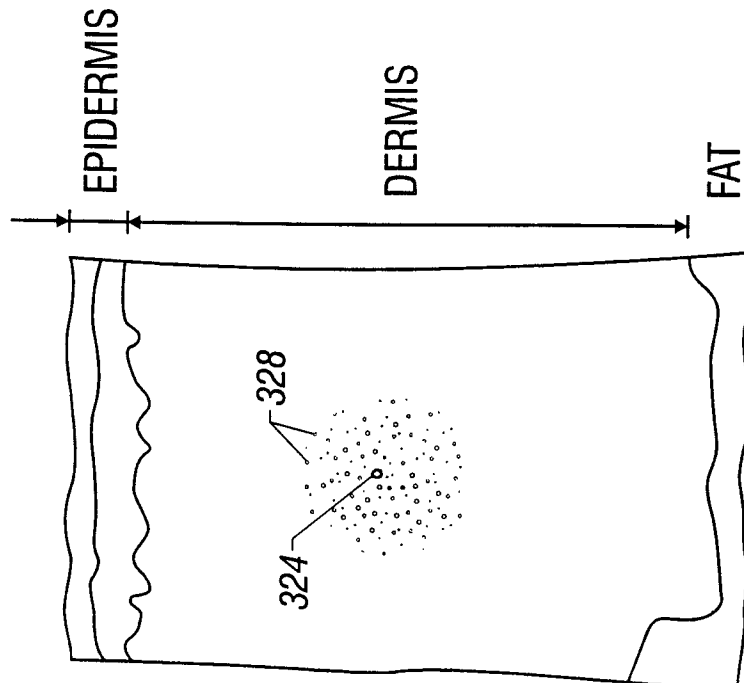


FIG. 31C

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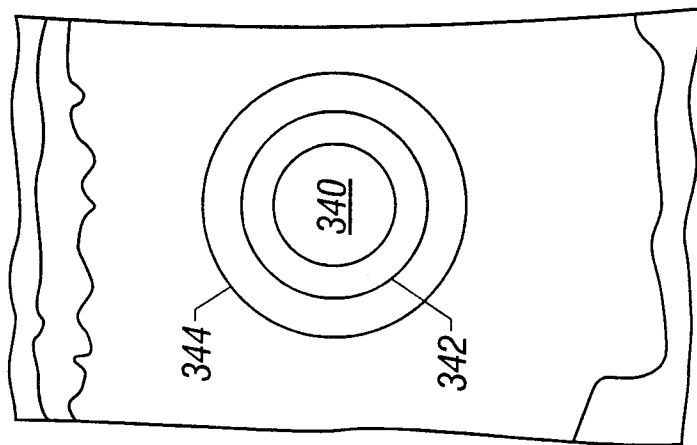


FIG. 31F

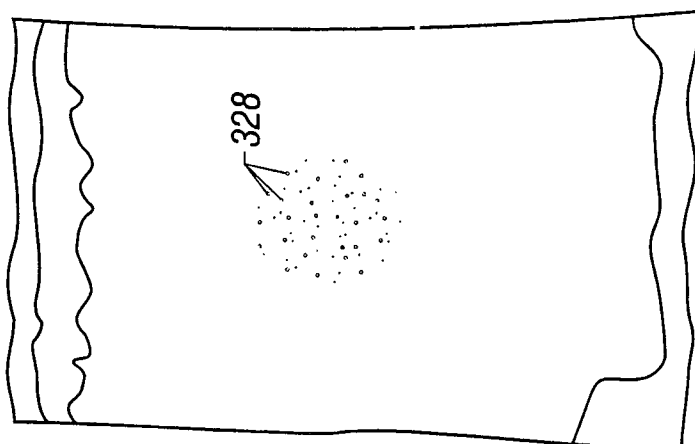
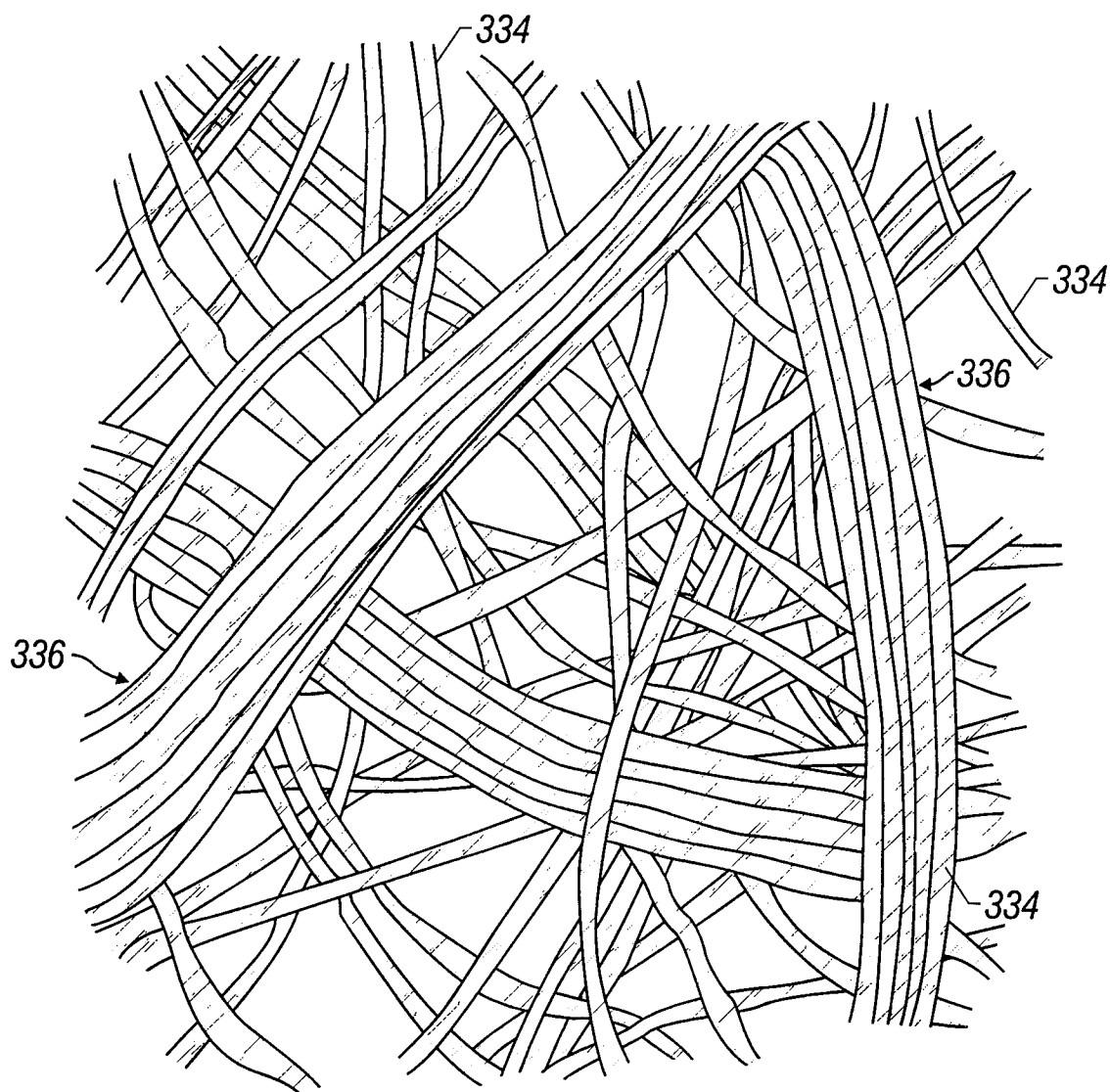
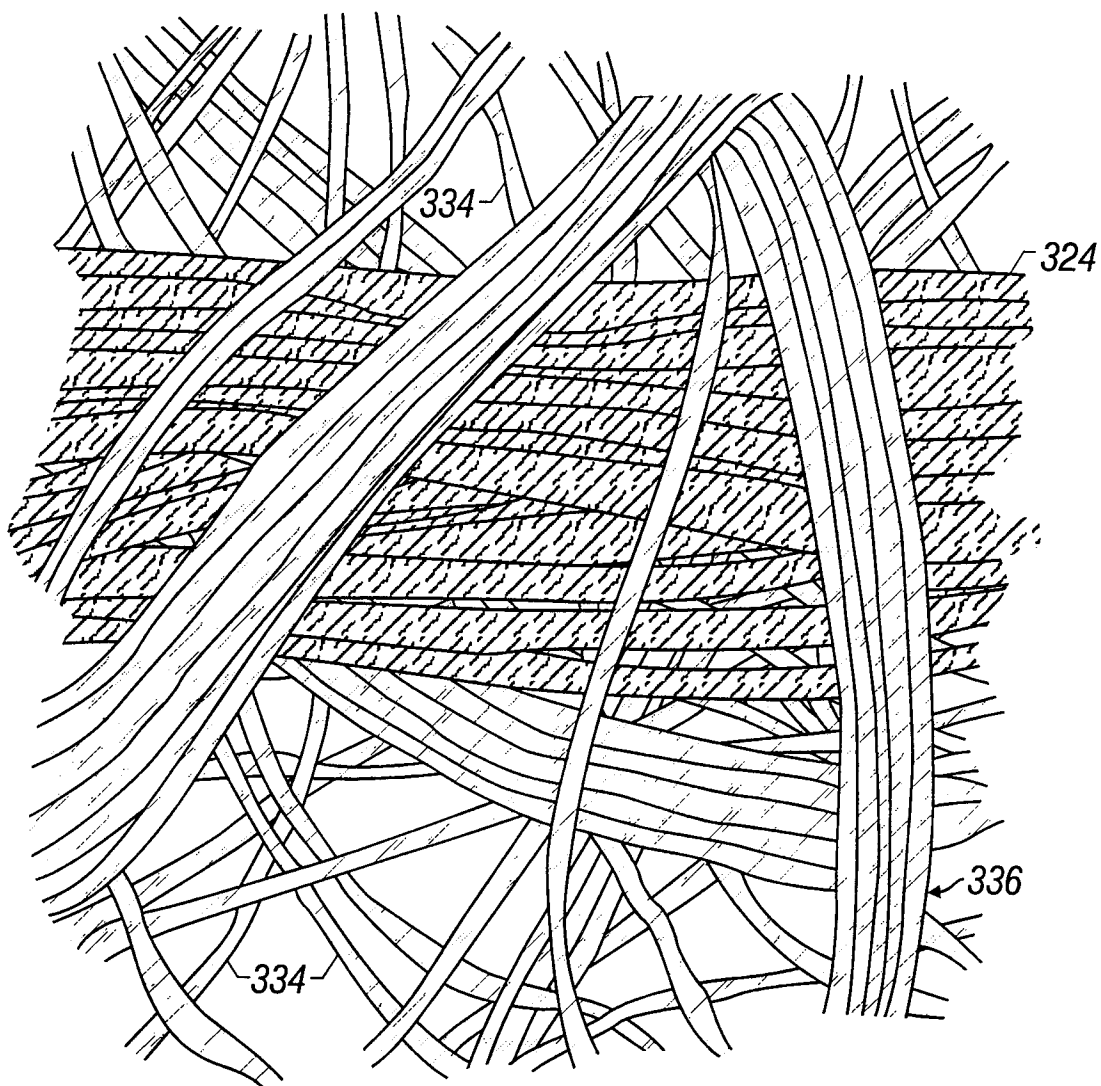


FIG. 31E

32/36**FIG. 32A**

33/36**FIG. 32B**

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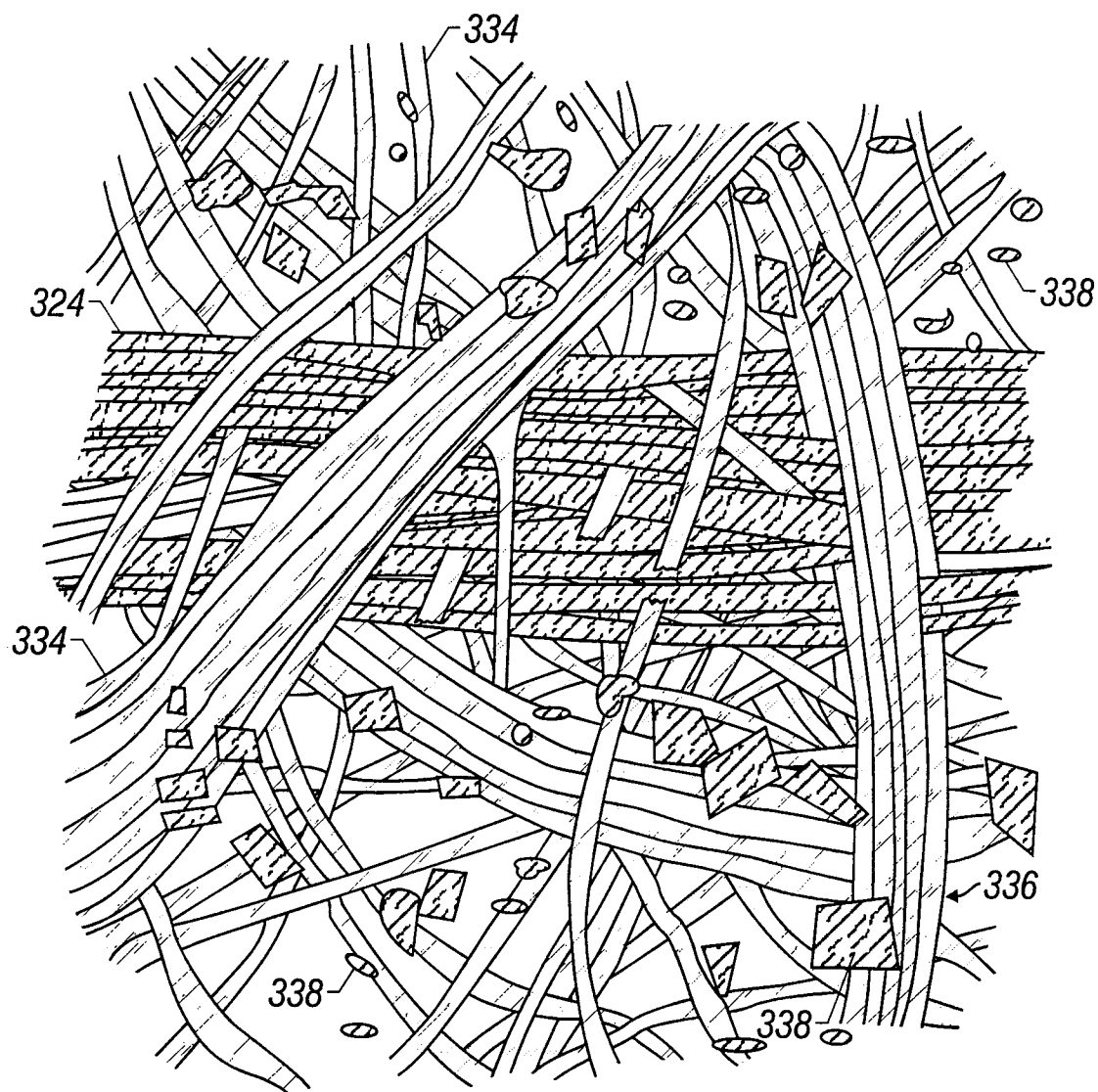


FIG. 32C

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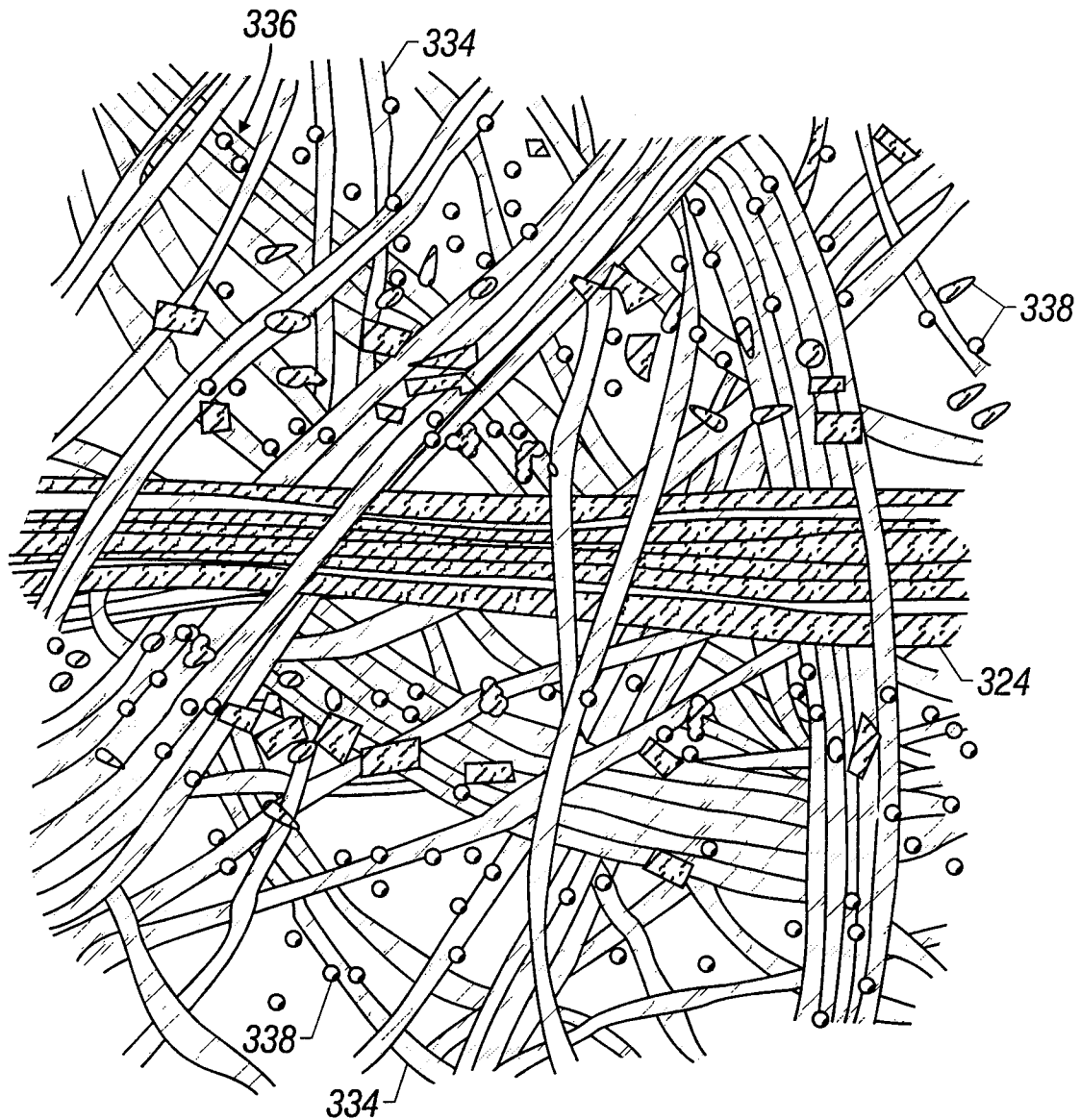
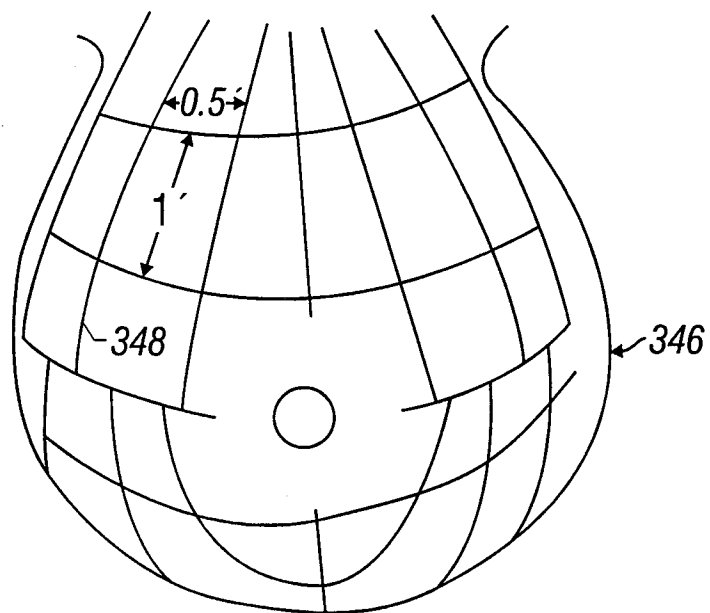
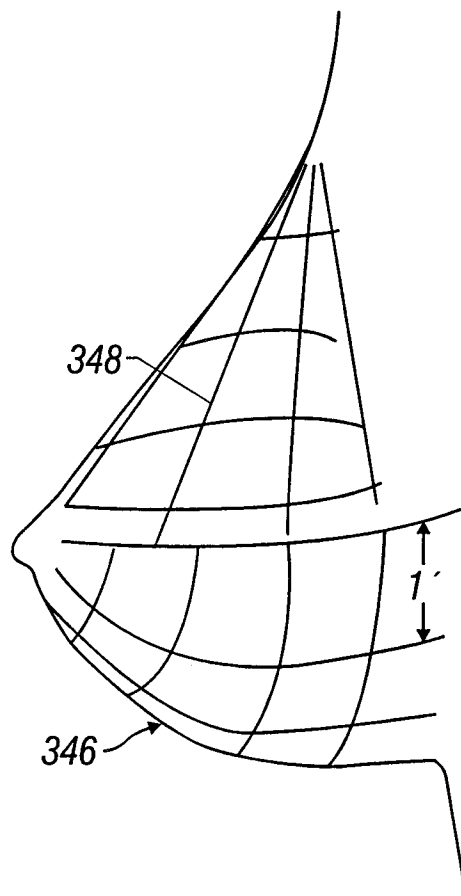


FIG. 32D

36/36**FIG. 33A**

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61B17/36

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 96 23447 A (ANDERSON ET AL.) 8 August 1996 see page 7, line 16-19 ---	8
Y	US 5 486 172 A (CHESS) 23 January 1996 see column 6, line 7-20 ---	8
A	WO 97 22384 A (LASER INDUSTRIES LTD) 26 June 1997 see page 10, line 7-17 ---	8
E	EP 0 827 716 A (KAMI) 11 March 1998 see claims 1,3 -----	8

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

3 August 1998

Date of mailing of the international search report

11. 11. 98

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

GLAS J.

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 1-7, 9, 10
because they relate to subject matter not required to be searched by this Authority, namely:
PCT Rule 39.1 (iv)
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. Claim: 8
2. Claim: 11

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9623447	A	08-08-1996	US 5595568 A	21-01-1997
			US 5735844 A	07-04-1998
			CA 2210720 A	08-08-1996
			CN 1172420 A	04-02-1998
			EP 0806913 A	19-11-1997

US 5486172	A	23-01-1996	US 5282797 A	01-02-1994
			US 5057104 A	15-10-1991
			AU 1609295 A	15-08-1995
			EP 0742703 A	20-11-1996
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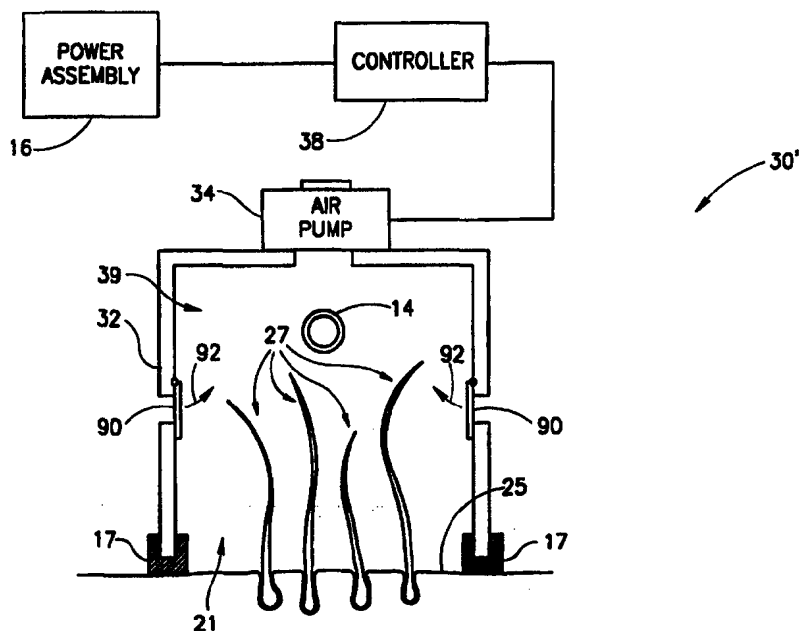
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(54) Title: APPARATUS AND METHOD FOR REMOVING HAIR



(57) Abstract

Apparatus for removing hairs (27) from a region of skin, the apparatus including: a housing (12) having an opening therein, the housing (12) forming a cavity enclosing a volume of air when the opening is placed in contact with the region of skin; a switchable heat source (14) disposed within the housing (12) that rapidly heats the volume of air to a temperature sufficient to destroy the hair (27) by conduction of heat along the length of the hair (27) to a follicle thereof; and a power source (16) that controllably energizes the heat source (14).

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APPARATUS AND METHOD FOR REMOVING HAIR

FIELD OF THE INVENTION

The present invention relates to apparatus and methods for hair removal.

BACKGROUND OF THE INVENTION

5 There are several types of devices for hair removal known in the art. One type includes mechanical devices used by a user to remove hairs by the user himself or herself. These include shavers and other mechanical devices. These mechanical devices are disadvantageous at least in two aspects, namely they remove the hairs for a relatively short time, and in most if not all cases they cause some degree of pain.

10 Other types of devices are directed to long term hair removal. Electrolysis devices are based on the use of "electric needles". Such fine needles are inserted into the hair follicle and apply an electric current to each hair. The current heats the hair and causes its carbonization and also heats the tissue near the hair causing its coagulation and partial or full coagulation of the blood capillaries which supply blood to the hair follicle. While such devices can result in
15 permanent hair removal, each hair must be treated individually, making hair removal by this method a tedious often painful, time consuming, and expensive.

 Another class of devices are Photothermolysis devices which are usually operated by physicians in clinics. These devices are based either on lasers (e.g. Ruby lasers) such as the laser device disclosed in U.S. Patent No. 5,059,192 to Zaias or an incoherent light source
20 coupled with filters and elaborate electronics to provide pulses of various durations and wave lengths as described in U.S. Patent No. 5,405,368 and European Patent publications EP 0 788 814 and EP 0 736 308 to Eckhouse. The Eckhouse documents teach heating the hair directly by a high flux of visible radiation that is absorbed by the hair follicles. Various filters and/or pulse lengths are used depending on the depth of penetration desired and the color of the hair being
25 removed.

SUMMARY OF THE INVENTION

 One aspect of some preferred embodiments of the invention provides an improved apparatus for hair removal. Some of these embodiments of invention may be used by a user to remove hair from his or her own body.

30 In a preferred embodiment of the invention, a cavity, is enclosed between a housing and a region of skin. A volume of air is enclosed within the cavity. The volume of air is heated by a fast heating source such as a flash lamp to provide a temperature high enough to kill any hair within the cavity. In a preferred embodiment of the invention, a heat gradient, having a higher temperature at the end of the air volume adjacent the flash lamp and a lower temperature at the

end of the air volume adjacent the skin, is formed. The parts of the hairs closer to the flash lamp are heated by the hot air resulting in removal of at least part of the hairs. Alternatively or additionally, the conduction of heat along the hair shafts heats the parts of the hairs sheathed within the hair follicles and the hair follicles which may further assist the hair removal by coagulating the capillary blood vessels supplying the hair follicles. This later heating preferably causes the hair to die, so that there is no regrowth.

In accordance with some preferred embodiments of the invention heating of the hairs and the region of skin underneath the apparatus is terminated at a selected time after flashing the flash lamp to prevent skin overheating. The termination of heating may be achieved by manually lifting the apparatus away from the skin or by automatically pumping air into the cavity at a selected time after the flashing of the flash lamp.

Additionally, the skin and portions of the hair within the follicles may be heated by broad band radiation emitted by the heat source (flash lamp). While this heating is not necessary for hair removal according to the invention, the irradiation may also assist in heating those parts of the hair shafts and the hair follicles and facilitate the heating of hair follicles to the coagulation temperature.

In accordance with preferred embodiments of the invention, means are provided for filtering the radiation to reduce the amount of low wavelength radiation from reaching the skin. Such low wavelength radiation is absorbed by hemoglobin in the blood and may destroy it.

There is thus provided, in accordance with a preferred embodiment of the invention, apparatus for removing hairs from a region of skin, the apparatus comprising:

- a housing having an opening therein, the housing forming a cavity enclosing a volume of air when the opening is placed in contact with the region of skin;

- a switchable heat source disposed within the housing which rapidly heats the volume of air to a temperature sufficient to destroy the hair by conduction of heat along the length of the hair to a follicle thereof; and

- a power source which controllably energizes the heat source.

Preferably, the heat source forms a temperature gradient between the source and the skin.

Preferably, the cavity is a sealed cavity.

In a preferred embodiment of the invention, the heat source also provides pulsed light that irradiate the region of skin, the light having an energy insufficient to destroy the hair.

Preferably, the pulsed light is a broad band pulsed light.

Preferably, the apparatus includes a filter disposed between the heat source and the opening which filters a preselected portion of the pulsed broad band light.

In a preferred embodiment of the invention, the heat source is a flash lamp or an arc discharge lamp. Preferably, the flash lamp comprises at least one glass xenon lamp. Preferably, the flash lamp comprises at least one quartz xenon flash lamp. Preferably, the at least one flash lamp comprises at least two lamps in series electrical connection. Preferably, the heat source is disposable.

In a preferred embodiment of the invention, the housing further comprises a sealing gasket attached to the housing along the circumference of the opening.

In a preferred embodiment of the invention, the apparatus includes a pump having a port communicating with the cavity. Preferably, the apparatus a controller that energizes the pump to reducing the air pressure within the air cavity to lift at least some of the hairs from the skin. Preferably, the controller causes energizing of the heat source after lifting at least some of the hair. Preferably the controller energizes the pump to exchange air within the cavity at a predetermined time after the heat source is energized.

In a preferred embodiment of the invention, the apparatus includes at least one valve that allows exchange of air within the cavity when the pump is energized. Preferably, the at least one valve is at least one one-way valve which allows air to enter the cavity when the pump is activated to draw air from the cavity. Alternatively, the pump pumps air into the cavity at the predetermined time.

Preferably, the apparatus includes a hair aligning member situated at the opening which raises at least some of the hairs from the skin. Preferably, the hair aligning member is a flat comb-like member or a flat perforated member. Preferably, the hair aligning member is made of a material which substantially blocks light having a wavelength lower than about 400 nanometers and substantially passes light having a wavelength higher than about 450 nanometers.

Preferably, the apparatus includes a reflector that reflects light produced by the heat source toward the skin. Preferably, the reflector substantially absorbs light having a wavelength lower than 400 nanometers.

In some preferred embodiments of the invention the apparatus includes an extension, the extension having a first end attachable to the opening and a second end placeable on the region of skin, the extension has an aperture therethrough defining an area for removing hairs.

Preferably, the housing is made of a heat insulating material.

In preferred embodiments of the invention, the power source is an electrical power source.

In preferred embodiments of the invention the apparatus fits into the palm of a hand.

There is further provided, in accordance with a preferred embodiment of the invention,
5 apparatus for removing hairs from a region of skin, the apparatus comprising:

a housing having an opening therein, the housing forming a cavity enclosing a volume of air when the opening is placed in contact with the region of skin;

a switchable energy source disposed within the housing which provides energy in an amount sufficient to destroy at least some of the hairs;

10 a power source that controllably energizes the heat source; and

a pump having a port communicating with the cavity.

Preferably, the apparatus includes a controller that energizes the pump to reducing the air pressure within the air cavity to lift at least some of the hairs from the skin. Preferably, the controller causes energizing of the energy source after lifting at least some of the hair.
15 Preferably, the controller energizes the pump to exchange air within the cavity at a predetermined time after the energy source is energized. Preferably, the apparatus includes at least one valve that allows exchange of air within the cavity when the pump is energized. Preferably the at least one valve is at least one one-way valve which allows air to enter the cavity when the pump is activated to draw air from the cavity. Preferably, the pump pumps air
20 into the cavity at the predetermined time.

There is further provided, in accordance with a preferred embodiment of the invention, a method for removing a plurality of hairs from a region of skin, each of the hairs having a first part disposed in a hair follicle within the skin and a second part distal of the skin, the method comprising:

25 selectively heating a portion of the second part of at least one of the plurality of hairs;

conducting heat from the second part to the hair follicle of the at least one of the plurality of hairs to thereby heat the hair follicle to a temperature high enough to cause the coagulation of the blood vessels supplying blood to the hair follicle.

Preferably, the method includes, prior to selectively heating:

30 irradiating the region of skin with a pulse of light to elevate the temperature of the first part of at least some of the hairs and of hair follicles of the at least some of the hairs to a first temperature, the first temperature being lower than the coagulation temperature of blood.

Preferably, the pulse of light is a broad band pulse of light. Preferably, the pulse of light is filtered to remove a preselected portion of the pulsed broad band light.

Preferably, the method includes keeping the temperature of the region of skin away from the hairs below the temperature required to coagulate blood.

In a preferred embodiment of the invention, selectively heating comprises:

5 providing a temperature gradient such that air in the vicinity of the second portion of the at least one hair is at a high temperature and air in the vicinity of the skin is below the temperature required to coagulate blood, except for heating of the immediate vicinity of the hair by conduction via the hair.

Preferably, selectively heating comprises flashing a flash lamp or an arc discharge lamp at a distance from the skin.

10 Preferably, selectively heating comprises:

providing a cavity overlying the region of skin, the cavity comprising a volume of air having a first end proximal to the region of skin and a second end distal to the region of skin;

15 heating the air in the cavity to create a temperature gradient in the volume of air, the temperature gradient having a first temperature at the first end and a second temperature at the second end, the first temperature being lower than the second temperature; and

maintaining the temperature gradient for a predetermined time interval sufficient for heating at least some of the plurality of hairs extending within the volume of air to a temperature sufficient to remove at least part of at least some of the plurality of hairs, while keeping the first temperature below the coagulation temperature of the region of skin.

20 There is further provided, in accordance with a preferred embodiment of the invention, a method for removing hairs from a region of skin, the region of skin having a plurality of hairs, each of the plurality of hairs includes a first part disposed in a hair follicle within the region of skin and a second part distal of the region of skin, the method comprising:

25 providing a cavity overlying the region of skin, the cavity comprising a volume of air having a first end proximal to the region of skin and a second end distal to the region of skin;

heating the air in the cavity to create a temperature gradient in the volume of air, the temperature gradient having a first temperature at the first end and a second temperature at the second end, the first temperature being lower than the second temperature; and

30 maintaining the temperature gradient for a predetermined time interval sufficient for heating at least some of the plurality of hairs extending within the volume of air to a temperature sufficient to remove at least part of at least some of the plurality of hairs, while keeping the first temperature below the coagulation temperature of the region of skin.

Preferably, the air cavity is a sealed air cavity.

Preferably, the method includes removing heat from the air after maintaining the temperature gradient, so as to keep the temperature of the skin below the coagulation temperature. Preferably, removing heat comprises cooling the air in the cavity. Preferably, cooling the air comprises removing air from the cavity.

5 In preferred embodiments of the invention, heating comprises providing a pulsed discharge.

Preferably the method includes heating the skin and the first part of the hair to a temperature below the coagulation temperature using electromagnetic radiation. Preferably, heating the skin and the first part of the hair includes filtering electromagnetic radiation to
10 produce a pulse of non-coherent, narrow band electromagnetic energy.

Preferably, heating comprises pulsing a flash lamp or an arc discharge lamp.

There is further provided, in accordance with a preferred embodiment of the invention, a method for removing hair by a person comprising:

applying heat from a portable hand held apparatus for hair removal, the apparatus
15 comprising a housing having an opening, a switchable heat source disposed within the housing and a power source that energizes the heat source,

characterized in that the heat generates a temperature gradient in an air volume enclosed in a cavity formed by placing the opening on a region of skin, the temperature gradient being suitable for hair removal.

20 Preferably applying of heat is performed by the person on his own skin.

The method preferably includes manually removing the opening of the housing from the region of skin.

There is further provided, in accordance with a preferred embodiment of the invention a method for hair removal by oneself comprising:

25 applying a heat pulse suitable for hair removal from a portable hand held apparatus, the applying performed by the person on his or her own skin.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention will be more clearly understood by the following description of non-limiting preferred embodiments of preferred embodiments of the invention described, with
30 reference to the accompanying drawings, in which like components are designated by like reference numerals, and wherein:

Fig. 1 is a perspective breakaway view illustrating a portable hand held device for hair removal in accordance with one preferred embodiment of the present invention;

Fig. 2 is a cross section illustration of the device of Fig. 1;

Fig. 3 is a cross section illustrating another implementation of the portable hand held device for hair removal, in accordance with another preferred embodiment of the present invention;

Fig. 4 is a schematic cross section illustration useful in understanding the method of operation of the device of Figs. 1 and 2, in accordance with a preferred embodiment of the invention;

Figs. 5A and 5B are schematic part cross-sectional partly functional diagrams illustrating portable hand held devices for hair removal, including an air pump for assisting the proper alignment of hairs in accordance with preferred embodiments of the present invention;

Fig. 6A is a perspective breakaway view illustrating a hair removal device having a comb like hair aligning member for alignment of hairs, in accordance with another preferred embodiment of the present invention;

Fig. 6B is a schematic cross section illustration useful in understanding the hair aligning action of the aligning member of the device of Fig. 6A;

Figs. 7 and 8 are schematic cross-sectional views of hair removal devices using a quartz flash lamp and different forms of filters for filtering the light pulse, in accordance with additional preferred embodiments of the present invention;

Fig. 9 is a schematic cross section illustrating a device for hair removal adapted for use with a plurality of differently shaped extenders, in accordance with yet another preferred embodiment of the present invention;

Figs. 10 -12 are schematic isometric views of three differently shaped extenders useful for hair removal when used with the hair removal device of Fig. 9; and

Figs. 13A and 13B are schematic drawings of excitation circuits and flash tube connections, in accordance with preferred embodiments of the invention.

DETAILED DESCRIPTION OF THE INVENTION

Reference is now made to Fig. 1 which is a pictorial illustration of a portable hand held device for hair removal, generally referenced 10, constructed and operative in accordance with an embodiment of the present invention and to Fig. 2 which is a cross section illustration of the device 10 of Fig. 1 taken along the lines II-II. Device 10 includes a housing 12, a flash lamp 14 for providing heat and a pulsed broad band light suitable for hair removal, and an assembly 16 for supplying power for energizing and controlling the application of power to flash lamp 14. Flash lamp 14 can be a xenon flash lamp having a glass tube, but can also be any other suitable flash lamp. Assembly 16 is preferably electrically connected to flash lamp 14 by electrically

conducting insulated wires 9. For the sake of clarity of illustration, wires 9 are not shown in Fig. 2. Housing 12 of device 10 has an opening 21 therein.

Housing 12 is preferably made of a thermally insulating material, for example, a high temperature plastic or a ceramic material. Housing 12 preferably has a sealing gasket 17 made from any suitable flexible material such as soft rubber for sealing the contact between housing 12 and a skin surface (not shown) on which opening 21 of housing 12 is placed before and during depilation. However, sealing gasket 17 is not critical to the operation of device 10. However, it is desirable that sealing be achieved by pressing opening 21 against the skin.

Housing 12 includes internal surfaces 15 that may be coated with a diffusely reflective coating (not shown) of high reflectivity such as a finely divided titanium dioxide based coating or any other suitable heat resistant highly reflective coating. As described below, coating that reflect IR well but do not reflect radiation having long wavelengths may advantageously be used.

Reference is now made to Fig. 3 which is a cross section illustrating another implementation of a portable hand held device 20 for hair removal, in accordance with another embodiment of the present invention. Device 20 is similar to device 10 except that it includes a reflector 13 within housing 12. Flash lamp 14 is disposed within reflector 13. For the sake of clarity of illustration, wires 9 between the flash lamp 14 and the assembly 16 are not shown in Fig. 3. Housing 12 of device 20 has an opening 23 therein, having the function of opening 21 of device 10.

Reference is now made to Fig. 4 which is a schematic cross section illustration useful in understanding the method of operation of the device of Fig. 2.

When opening 21 of device 10 is placed on skin 25, a sealed air cavity 11 is formed between housing 12 and skin 25. Sealed air cavity 11 contains a volume of air 26. Sealing of the cavity is desirable and is preferably achieved by pressing gasket 17 against skin 25.

The region of skin 25 covered by opening 21 includes a plurality of hairs 27. Each of hairs 27 has a first part 31 which is disposed within hair follicles 33 and a second part 29 protruding outside of skin 25 in a direction generally distal from the surface of skin 25.

A user activates device 10 by energizing flash lamp 14. For example, device 10 may be activated by the user by pressing a button (not shown) or activating a switch (not shown) positioned on assembly 16 or on any other suitable part of the device 10. When assembly 16 energizes flash lamp 14, flash lamp 14 produces a broad band light pulse having an approximate duration of 1-75 milliseconds and an energy density of preferably between 1.5 to 5 Joule/cm² measured on the skin.

The light pulse irradiates the region of skin 25 underlying opening 21 of housing 12. The light pulse also irradiates hairs 27. A part of the light pulse is absorbed by melanin pigment in hairs 27. Another smaller part of the light pulse is absorbed by the region of the skin 25 directly underneath the opening 21. In preferred embodiments of the invention, the amount of energy pulsed through the flash lamp 14 is such that the absorption of the light by the region of skin 25 raises the temperature of the region of skin 25. However, this temperature is preferably lower than the coagulation temperature of blood. Preferably, the temperature of hair follicles 33 and skin 25 due to the absorption of radiation from the light pulse should not exceed 50 - 65°C. Since most of the radiation from flash lamp 14 is absorbed by the melanin in the hair while only a small portion of the radiation is absorbed by the skin tissue, skin tissue which is more than about 0.2 mm from hair follicles 33 is heated negligibly.

About half of the electrical energy used to energize flash lamp 14 is wasted to heat the flash lamp itself, heating flash lamp 14 to a much higher temperature than that of air volume 26 surrounding the flash lamp 14. Typically, in glass flash lamps the temperature of the flash lamp may reach a temperature between 600 -800°C and in quartz flash lamps the temperature of the flash lamp may reach a temperature between 1200 -1600°C. The maximal temperature of the flash lamp is typically reached within 1-2 milliseconds.

The air immediately adjacent to the flash lamp 14 is heated by the flash lamp. Heat is conducted by convection from air adjacent flash lamp 14 to air which is further away from flash lamp 14, creating a temperature gradient in the air contained in cavity 11.

The temperature of the air close to the flash lamp will be the highest and will decrease as the distance from flash lamp 14 increases. Since each of hairs 27 protrudes from skin 25 along the sealed air cavity 11 in the general direction of the flash lamp 14, those parts of hairs 27 that are closer to flash lamp 14 will be exposed to air having a higher temperature than the parts of the same hairs which are closer to skin 25. Thus, the part of a hair 27 closer to the flash lamp will be heated by the hot air to a higher temperature than the part of the same hair which are closer to skin 25. Heat will be conducted from the hotter parts of hair 27 towards first part 31 of hair 27. The heat flow will increase the temperature of first part 31 and hair follicle 33 surrounding it to a temperature of approximately 70-100°C which is sufficient to cause the coagulation of the blood capillaries supplying blood to hair follicle 33.

Additionally, the temperature reached by many of the hairs at parts which are closer to the flash lamp are sufficiently high to cause burning or carbonization of a substantial portion of the hair thus effectively removing a substantial portion of the hair.

It is noted that, it is not necessary to shave hairs 27 prior to hair removal by the methods of the present invention. However, if the hair is cut, shaved or otherwise shortened, It was found that hairs that have a shaft protruding roughly 2 mm or more from the skin surface in the general direction towards flash lamp 14 are removed more effectively by the device.

5 The heat gradient in the volume of air 26 within air cavity 11 tends to equilibrate so that the air temperature near the surface of the region of skin 25 rises with time after the energizing of flash lamp 14. To prevent the temperature of the skin from rising above 70°C, housing 12 may be lifted away from skin 25. Lifting of housing 12 causes opening of air cavity 11 and prevents excess heating of the skin 25 allowing air at room temperature to contact the skin.
10 Alternatively or additionally, the heated air may be removed from the cavity.

It is noted that, typically, hairs 27 are not necessarily aligned perpendicularly to the surface of the skin. Hairs which are lying in a general direction parallel to the surface of the skin 25 will reach a temperature lower than hairs which are generally aligned perpendicular to the surface of the skin. Thus, it may be desirable to align as many of hairs 27 as possible in a
15 direction generally perpendicular to the surface of the skin.

Reference is now made to Fig. 5A which is a schematic partly cross-sectional partly functional diagram illustrating a portable hand held device 30 for hair removal, having an air pump 34 for assisting the proper alignment of hairs in accordance with a preferred embodiment of the present invention. Device 30 includes a flash lamp 14 disposed within a housing 32 and
20 an assembly 16 for energizing the lamp 14. Housing 32 has an opening 21 and differs from housing 12 of Fig. 1 in that it is connected to air pump 34, for example by a tube 36. Air pump 36 is preferably an electrical air pump but can be any other suitable small air pump.

Device 30 further preferably includes a controller 38 suitably connected to air pump 36 and to e assembly 16. Controller controls the timing of activation of air pump 36 and the timing
25 of the energizing of flash lamp 14 by assembly 16. Controller 38 may also include a power source (not shown) for supplying power to air pump 36. The power source may be an electrical battery, a mains operated power supply or any other suitable power source. Alternatively, the power to operate air pump 36 may be supplied by a power source (not shown) included within assembly 16 and also used for energizing flash lamp 14. Air pump 36 is preferably a reversible
30 air pump. Reversing the direction of pumping respectively reverses the flow of air into and out of the cavity.

Device 30 is operated by placing opening 21 of the housing 32 on a region of skin 25 to be depilated and activating controller 38. In a preferred embodiment of the invention, controller 38 first activates air pump 36 to pump some of the air out of a sealed air cavity 39 formed

between housing 32 and the region of skin 25 adjacent opening 21. The pumping action causes the erection of at least some of hairs 27 so that they do not lie against the skin by applying a gentle suction action to the region. This first action of the pump is desirable, but not essential for operation of the device.

5 After partial alignment of the hairs is achieved, the pump is preferably turned off and controller 38 activates assembly 16 to energize flash lamp 14. The light and heat pulse generated by flash lamp 14 operate to remove at least part of the hairs 27 as disclosed above in detail for the device 10 of Fig. 1. After the hair removing action is achieved and before the temperature of the region of skin 25 exceeds a value that might cause a skin burn (which is
10 roughly 0.5 seconds after energizing flash lamp 14), controller 38 automatically reverses the direction of air pumping by air pump 36. This reversal pumps air at room temperature from outside of the device 30 into the housing 32, dissipates the heat within the housing by displacing the volume of air within it with air at room temperature. The flow of air also cools the region of skin 25 to prevent the development of a skin burn.

15 Fig. 5B shows a hair removal device 30' in accordance with an alternative preferred embodiment of the invention. While suction is shown as being applied at the side of the cavity in Fig. 5A, it is more effectively applied at or near the top of the housing, as shown in Fig. 5B. Furthermore, while, as shown in Fig. 5A, the hot air must leave the housing via opening 21, valved openings 90 (which open in direction 92) are provided on the side walls of the housing
20 in Fig. 5B to aid in the entry of fresh air into the cavity and removal of air from the cavity by pump 36. In this embodiment, pump 36 is preferably a purely suction pump. In operation the pump is preferably activated before the flash to raise the hair from the skin. Then the pump operation is interrupted and the lamp is flashed. After a short time the pump is activated again to bring fresh air into the cavity and remove heat from the cavity and from the flash lamp. The
25 time between the flashing of the lamp is such that the hair has enough time to conduct the heat to the follicle and heat it to the proper temperature for coagulation but not so long that the heat from the lamp reaches the skin to the extent that it causes burning or even, preferably, any discomfort. This time is in the order of 0.1-2 seconds, more preferably 0.2-1 seconds and most preferably about 0.5 seconds. It should be noted that the valves are kept closed immediately
30 after flashing by the pressure build-up of the heat in the cavity.

 Devices 30 and 30' have the advantage of improving the efficiency of hair removal by improving the hair alignment and also has the advantage of being automatic obviating the need of timely manual lifting of the device by the user.

Additional methods of hair alignment are also possible. Reference is now made to Figs. 6A and 6B. Fig. 6A is a schematic perspective breakaway view of a hair removal device 40 having a comb like hair aligning member 42 for hair alignment, in accordance with another preferred embodiment of the present invention.

5 Device 40 is similar to device 10 of Fig. 1 except that device 40 includes hair aligning member 42 spanning across part of opening 21. Preferably, hair aligning member 42 is a flat thin comb-like member made from a metal such as stainless steel or from any other suitable material such as another metal, plastic, a ceramic material and the like. In a preferred embodiment of the invention hair aligning member 42 includes a plurality of teeth 44 separated
10 by a plurality of narrow gaps 46. Typically, the width of the teeth 44 is approximately 0.7 millimeters and the width of the gaps 46 is approximately 0.2 millimeters. However, these dimensions may be varied to accommodate different hair thicknesses. Furthermore, the hair aligning member 42 may be detachably attached to the housing 12 to facilitate quick attachment of various differently shaped hair aligning members (not shown) by the user.

15 Hair aligning member 42 may be attached to housing 12 such that when sealing gasket 17 is placed in contact with the skin, teeth 44 contact the skin. Alternatively, hair aligning member 42 may be attached to housing 12 such that when sealing gasket 17 is placed in contact with the skin, teeth 44 do not contact the skin and are positioned a small distance above the skin.

20 When device 40 is used for removing hair it is placed on the skin so that sealing gasket 17 contacts the skin. Device 40 is moved along the skin in a direction parallel to the orientation of teeth 44 as indicated by an arrow 47. This movement of device 40 along the skin causes some of the hairs (not shown) to enter gaps 46 and improves their alignment in a direction roughly perpendicular to the surface of the skin.

25 After hair alignment, device 40 (whose internal structure may differ from that shown in Fig. 6A and may have features shown in other Figs.) is operated to remove hair as disclosed above. These actions of hair aligning followed by hair removing may be then repeated by the user either of the same skin area or on a different skin area.

30 Fig. 6B is a schematic cross sectional view illustrating of device 40 of Fig. 6A positioned over a region of skin 25. Some of hairs 27 are shown disposed in gaps 46 between different pairs of teeth 44. When device 40 is moved along the skin, comb like member 42 aligns and raises some of hairs 27 to facilitate hair removal.

It is noted that while hair aligning member 42 is shaped like a comb, other implementations of the hair removal device may have other different forms of hair aligning

members. For example, the hair aligning members may be constructed in the shape of flat flexible perforated metal sheets (not shown) having a plurality of openings therethrough such as the hair aligning members known in the art and used in electrical shaving machines. The construction of such aligning members is well known to those skilled in the art and will
5 therefore not be further described.

It is further noted that, the methods of hair removal disclosed hereinabove may also be applied to skin without including the first step of photothermal heating of the hair portions within the follicles to a temperature of between 50-65°C as described above. While the selective heating of the hairs and hair follicles to a sub-coagulation temperature may improve
10 the efficiency of hair removal, hairs can also be removed by the air heating action and subsequent burning and/or carbonization of the hairs caused by the heating of the hair shafts due to the hot air within the sealed air cavity. Thus, hair can still be efficiently removed even in situations where the broad band light pulse from the flash lamp 14 does not efficiently reach the part of the hair shaft which is sheathed within the hair follicle because of partial or full blocking
15 of the light pulse by the hair aligning member 42 or by other different forms of hair aligning members used in different embodiments of the present invention.

It is still further noted that while the preferred embodiments of the hair removing device disclosed above are implemented using a glass xenon flash lamp, the life span of the flash lamp may be significantly improved by using a quartz xenon flash lamp. However, unlike the light
20 generated by glass xenon flash lamps which does not include substantial ultraviolet (UV) radiation (due to the absorbence of UV radiation by the glass tube of the xenon flash lamp), the light generated by quartz xenon flash lamps includes UV light radiation in the spectral range between 200-400 nanometers that may cause damage to the skin tissue. When such quartz flash lamps are used, the light pulsed from the flash lamp has to be filtered to remove the undesirable
25 portion of the UV radiation from the light reaching the skin. For example, if a comb member as shown in Figs. 6A and 6B is used, it may be made of orange or red colored perspex which blocks at least part of such light.

Reference is now made to Figs. 7 and 8 which are schematic cross-sectional views of hair removal devices using different forms of filters for filtering the light pulse, in accordance
30 with additional preferred embodiments of the present invention.

Fig. 7 illustrates a hair removal device 50. Device 50 is similar to device 10 of Figs. 1 and 2, except that device 50 uses a quartz flash lamp 54 instead of glass flash lamp 14 of device 10 and includes a filter 56 for filtering out the undesired UV radiation emitted by quartz flash lamp 54. Filter 56 can be a model 450FH90-25 long wave pass filter commercially available

from Andover Corporation, NH, USA or merely a colored plastic. This long wave pass filter absorbs most of the radiation having a wavelength below 450 nanometers while transmitting most of the radiation having a wavelength above 450 nanometers.

Filter 56 may be any other suitable filter having the proper absorption properties to
5 absorb the undesirable UV radiation while passing longer wavelengths of radiation, and having a sufficiently high thermal conductivity and a sufficiently low thermal mass to assure a high rate of heat flow from flash lamp 54 and the hot air surrounding it to filter 56 and the subsequent heat flow from filter 56 to air adjacent side 56A of filter 56 facing towards the opening 21. Device 50 is used for hair removal as described above for device 10 except that the
10 heat generated by pulsing the flash lamp 54 has to flow through UV filter 56 to form a temperature gradient in the sealed air cavity enclosed within filter 56, the walls of housing 12 and the skin on which the device 50 is placed.

It is noted that quartz xenon flash lamps may reach an initial temperature of 1200-1600°C after pulsing. These temperatures which are higher than those attained by glass xenon
15 flash lamps may compensate for the presence of filter 56.

It is further noted that, while filter 56 of Fig. 7 is flat, filter 56 may have other suitable shapes and geometry. For example, filter 56 may be concave or convex.

Fig. 8 illustrates a hair removal device 60 which is similar to the device 50, except that instead of the flat filter 54 of Fig. 7 device 60 includes a cylindrical filter 66 attached to
20 housing 12. Quartz flash lamp 54 is disposed within cylindrical filter 66 for filtering the broad band light generated by the flash lamp 54 as disclosed above.

As indicated above, the use of a comb with filtration properties may obviate the need for an additional filter.

The devices disclosed above may be used for removing hair from various body regions
25 of the user such as the hands, legs face and other body regions. It is therefore desirable to provide the device of the present invention with a way of adapting the device for removing hair from body regions having different sizes and shapes.

Reference is now made to Fig. 9, which is a schematic cross section illustrating a device for hair removal 70 adapted for use with a plurality of differently shaped extenders, in
30 accordance with a preferred embodiment of the invention. Device 70 includes a housing 15 having a raised collar 17. Device 70 further includes a quartz flash lamp 54 and an assembly 16 for energizing flash lamp 54 and for controlling the operation as disclosed above. Device 70 also includes a UV filter 56 attached to housing 15 as disclosed above. An extender 63 is

detachably attached to housing 17. In a preferred embodiment of the invention extender 63 is attached to housing 15 by forcing the extender over raised collar 17.

Extender 63 is a preferably hollow and has a first end 63A attachable to the raised collar 17 and a second end 63B for contacting the skin. Extender 63 preferably has an aperture 19 defining an area for removing hairs. In one embodiment of the invention, extender 63 is a metal extender. However, extender 63 is desirably made of a thermally insulating material such as a plastic or a ceramic material. Device 70 is operated by pressing aperture 19 against the skin and energizing quartz flash lamp 54 as disclosed above.

It is noted that many different forms of extender 63 can be made, each having an aperture of a different shape and/or size for adapting device 70 for removing hair from different regions of skin of different organs such as the face the limbs and the like.

Reference is now made to Figs. 10-12 which are schematic isometric views of three differently shaped extenders 65, 67 and 69 useful for hair removal when used with the hair removal device 70 of Fig. 9. Fig. 10 illustrates an extender 65 having a rectangular aperture 75. Fig. 11 illustrates an extender 67 having an ellipsoidal aperture 77. Fig. 12 illustrates an extender 69 having a circular aperture 79. Each of extenders 65, 67 and 69 may be used with device 70 for removing hair from various skin regions.

It is noted that, extenders 63, 65, 67 and 69 of Figs. 9-12, respectively, may also include a sealing gasket (not shown) attached to the end of the extender distal from device 70 and made from a soft resilient material such as soft rubber for better sealing of the contact region with the skin. Extenders 63, 65, 67 and 69 of Figs. 9-12, respectively may or may not be internally coated as described above.

In accordance with a preferred embodiment of the present invention, flash lamps 14 and 54 may be disposable to allow convenient replacement of the lamp once it is burnt out.

It is noted that, while the preferred embodiments of the hair removing devices of Figs. 1-9 have a housing shaped generally as a rectangular open box, other embodiments are possible in which the housing has other shapes such as a cylindrical shape, a triangular prism shaped open box, a truncated triangular prism shaped open box or any other suitable shape having an open side and capable of forming a sealed cavity when suitably placed on the skin.

A preferred embodiment of the assembly 16 as shown in Fig. 13A, comprises two capacitors 100 and 102, a charging resistor 103, a power source 104, a thyristor or other switch 106 and a trigger transformer 108. Such assemblies for energizing flash lamps (and other suitable assemblies) are well known in the art and will not be described further. For example, a suitable flash lamp assembled together with assembly 16 is commercially available from All

Electronics Corporation, CA, USA, as flash assemblies under catalog numbers FSH-1 and FSH-4. In the FSH-1 flash assembly, flash lamp 14 is assembled with part of assembly 16 wherein a battery is wired thereto. In the FSH-4 all components are connected to an assembly platform including flash lamp 14 and a battery.

5 It is noted that, while the above commercially available flash assemblies FSH-1 and FSH -4 can be used to implement the present invention, other suitable commercially available systems can be used or modified to make them suitable for use in the present invention by changing any of their components to control the flow of electrical energy flowing through the flash lamp 14. Alternatively the assembly 16 may be constructed from commercially available
10 electrical and electronic parts and commercially available flash lamps.

For example, an embodiment of the hair removing device of the present invention was constructed by modifying commercially available components. The device was built by modifying a model INSTAFLASH 80 electronic flash unit (for use on Kodak Ek-8 instant cameras), commercially available from SUNPAK CORPORATION, Tokyo, Japan. The
15 electronic assembly for energizing the unit included, *inter alia*, an electrolytic capacitor having a capacitance of 750 microfarads (rated at 300 Volts). To increase the total charge available for discharging the flash lamp, six additional electrolytic capacitors, each having a nominal capacitance of 410 microfarads (rated at 300 Volts) were electrically connected in parallel with the 750 microfarads capacitor, increasing the total capacitance to a nominal value of 3210
20 microfarads (rated at 300 Volts).

The original reflector and flash lamp of the flash unit were replaced with a model A1033 flash tube with reflector, commercially available from The Electronic Goldmine, Arizona, USA The flash lamp is 1.75 inches long and the reflector has a rectangular opening having the dimensions of approximately 21 by 44.3 mm. The approximate distance from the
25 center of the flash lamp to the center of the area defined by the opening of the reflector is 14 mm. The reflector is made of a plastic material with a reflective coating. The calculated electrical energy stored by the capacitors of the modified unit is approximately 144 joule. It is estimated that more than 50% of this energy is converted to heat during the flashing of the flash lamp. The modified flash unit was powered by four standard AA size 1.5 volt alkaline batteries or ,alternatively, by a commercial 6 volts, 2 amperes DC power supply. Both power sources
30 gave essentially similar results.

The opening of the reflector was placed in contact with the skin of the hand of one of the inventors of the present invention by lightly pressing the reflector against the skin and the flash unit was activated to energize the flash lamp. The reflector was lifted from the skin at

about 0.5 seconds after the activation of the flash unit. It was found that lifting of the reflector from the skin at about 0.5 seconds after the activation of the flash lamp unit, results in efficient hair removal while preventing any pain sensation and undue heating of the region of skin 25 which was under the opening. However, It is noted that the optimal time of lifting of the device may vary in different embodiments of the device and may depend, *inter alia*, on the size and shape of the housing (or reflector), the distance of the flash lamp from the skin, the maximal temperature reached by the flash lamp, the degree of skin pigmentation and the particular region of skin which is being treated.

In a preferred embodiment of the invention, as shown in Fig. 13B, a plurality of flash lamps are used, preferably connected in series. This embodiment results in a longer flash time, substantially equal to about twice the flash time when a single tube is used. However, when two tubes are used, the spectrum is shifted toward higher wavelengths and a lower radiation power density at the skin results. The heat generation remains practically the same as when a single tube is used.

It is noted that the devices disclosed herein are only given by way of example and are not intended to limit the scope of the present invention. The structure and dimensions of the devices and the above disclosed parameters for activating and using the devices may be changed and modified according to the desired implementation of the device and may depend, *inter alia*, on the type and size of the flash lamp, the electrical charge required for pulsing the flash lamp, the type size and reflectivity of the reflector, the dimensions of the opening of the reflector or housing of the device and on the skin pigmentation of the person using the devices. Furthermore, features shown in the various embodiments of the invention may be combined and/or omitted in other embodiments of the invention.

It is further noted that, any of devices for removing hairs 10, 20, 30, 40, 50, 60 and 70 described above may also include a device housing to which the various components of each device are attached. For example, the power assembly 16 and the housing 12 of the device 10 may be attached to a device housing. Similarly, the power assembly 16, the controller 38, the housing 32 and the air pump 34 of the device 30 (Fig. 5), may all be attached to a device housing.

It will be appreciated that device 10, being a hand held, portable device directed for use by the user himself, has a size which allows it to fit into the palm of a hand. However, other preferred embodiments of the present invention are possible which are larger and do not fit in the palm of the hand.

It will be appreciated by the person skilled in the art that the invention is not limited to what has been shown above. While the invention has been described with respect to a limited number of embodiments, it will be appreciated that many variations, modifications and other applications of the invention may be made.

- 5 The terms "include" and "comprise" and their conjugations, when used in the claims, mean "including, but not necessarily limited to."

CLAIMS

1. Apparatus for removing hairs from a region of skin, the apparatus comprising:
a housing having an opening therein, the housing forming a cavity enclosing a volume
5 of air when the opening is placed in contact with the region of skin;
a switchable heat source disposed within the housing that rapidly heats the volume of air
to a temperature sufficient to destroy the hair by conduction of heat along the length of the hair
to a follicle thereof; and
a power source that controllably energizes the heat source.
10
2. Apparatus according to claim 1 wherein the heat source forms a temperature gradient
between the source and the skin.
3. Apparatus according to claim 1 or claim 2 wherein the cavity is a sealed cavity.
15
4. Apparatus according to any of the preceding claims wherein the heat source also
provides pulsed light that irradiate the region of skin, the light having an energy insufficient to
destroy the hair.
- 20 5. Apparatus according to claim 4 wherein the pulsed light is a broad band pulsed light.
6. Apparatus according to claim 4 or claim 5 and including a filter disposed between the
heat source and the opening which filters a preselected portion of the pulsed broad band light.
- 25 7. Apparatus according to any of the preceding claims wherein the heat source is a flash
lamp or an arc discharge lamp.
8. Apparatus according to claim 7 wherein the flash lamp comprises at least one glass
xenon lamp.
30
9. Apparatus according to claim 7 wherein the flash lamp comprises at least one quartz
xenon flash lamp

10. Apparatus according to claim 8 or claim 9 wherein the at least one flash lamp comprises at least two lamps in series electrical connection.
11. Apparatus according to any of claims 7-9 wherein the heat source is disposable.
- 5 12. Apparatus according to any of the preceding claims wherein the housing further comprises a sealing gasket attached to the housing along the circumference of the opening.
- 10 13. Apparatus according to any of the preceding claims and including a pump having a port communicating with the cavity.
14. Apparatus according to claim 13 and including a controller that energizes the pump to reducing the air pressure within the air cavity to lift at least some of the hairs from the skin.
- 15 15. Apparatus according to claim 14 wherein the controller causes energizing of the heat source after lifting at least some of the hair.
- 20 16. Apparatus according to any of claims 13-15 and including a controller that energizes the pump to exchange air within the cavity at a predetermined time after the heat source is energized.
17. Apparatus according to claim 16 and including at least one valve that allows exchange of air within the cavity when the pump is energized.
- 25 18. Apparatus according to claim 17 wherein the at least one valve is at least one one-way valve which allows air to enter the cavity when the pump is activated to draw air from the cavity.
- 30 19. Apparatus according to claim 13 or claim 14 wherein the pump pumps air into the cavity at the predetermined time.
20. Apparatus according to any of the preceding claims including a hair aligning member situated at the opening which raises at least some of the hairs from the skin.

21. Apparatus according to claim 20 wherein the hair aligning member is a flat comb-like member or a flat perforated member.
22. Apparatus according to claim 20 or claim 21 wherein the hair aligning member is made
5 of a material which substantially blocks light having a wavelength lower than about 400 nanometers and substantially passes light having a wavelength higher than about 450 nanometers.
23. Apparatus according to any of the preceding claims and including a reflector that
10 reflects light produced by the heat source toward the skin.
24. Apparatus according to claim 23 wherein the reflector substantially absorbs light having a wavelength lower than 400 nanometers.
25. Apparatus according to any of the preceding claims and comprising an extension, the
15 extension having a first end attachable to the opening and a second end placeable on the region of skin, the extension has an aperture therethrough defining an area for removing hairs.
26. Apparatus according to any of the preceding claims wherein the housing is made of a
20 heat insulating material.
27. Apparatus according to any of the preceding claims wherein the power source is an electrical power source.
28. Apparatus according to any of the preceding claims, which apparatus fits into the palm
25 of a hand.
29. Apparatus for removing hairs from a region of skin, the apparatus comprising:
a housing having an opening therein, the housing forming a cavity enclosing a volume
30 of air when the opening is placed in contact with the region of skin;
a switchable energy source disposed within the housing which provides energy in an amount sufficient to destroy at least some of the hairs;
a power source that controllably energizes the heat source; and
a pump having a port communicating with the cavity.

30. Apparatus according to claim 29 and including a controller that energizes the pump to reducing the air pressure within the air cavity to lift at least some of the hairs from the skin.
- 5 31. Apparatus according to claim 30 wherein the controller causes energizing of the energy source after lifting at least some of the hair.
32. Apparatus according to any of claims 29-31 and including a controller that energizes the pump to exchange air within the cavity at a predetermined time after the energy source is energized.
- 10 33. Apparatus according to claim 32 and including at least one valve that allows exchange of air within the cavity when the pump is energized.
- 15 34. Apparatus according to claim 33 wherein the at least one valve is at least one one-way valve which allows air to enter the cavity when the pump is activated to draw air from the cavity.
35. Apparatus according to claim 32 or claim 33 wherein the pump pumps air into the cavity at the predetermined time.
- 20 36. A method for removing a plurality of hairs from a region of skin, each of the hairs having a first part disposed in a hair follicle within the skin and a second part distal of the skin, the method comprising:
- 25 selectively heating a portion of the second part of at least one of the plurality of hairs;
- conducting heat from the second part to the hair follicle of the at least one of the plurality of hairs to thereby heat the hair follicle to a temperature high enough to cause the coagulation of the blood vessels supplying blood to the hair follicle.
- 30 37. A method according to claim 36 and including, prior to selectively heating:
- irradiating the region of skin with a pulse of light to elevate the temperature of the first part of at least some of the hairs and of hair follicles of the at least some of the hairs to a first temperature, the first temperature being lower than the coagulation temperature of blood.

38. A method according to claim 37 wherein the pulse of light is a broad band pulse of light.
39. A method according to claim 38 wherein the pulse of light is filtered to remove a
5 preselected portion of the pulsed broad band light.
40. A method according to any of claims 36-39 and including keeping the temperature of the region of skin away from the hairs below the temperature required to coagulate blood.
- 10 41. A method according to any of claims 36-40 wherein selectively heating comprises:
providing a temperature gradient such that air in the vicinity of the second portion of the
at least one hair is at a high temperature and air in the vicinity of the skin is below the
temperature required to coagulate blood, except for heating of the immediate vicinity of the hair
by conduction via the hair.
- 15 42. A method according to any of claims 36-41 wherein selectively heating comprises
flashing a flash lamp or an arc discharge lamp at a distance from the skin.
43. A method according to any of claims 36-42 wherein selectively heating comprises:
20 providing a cavity overlying the region of skin, the cavity comprising a volume of air
having a first end proximal to the region of skin and a second end distal to the region of skin;
heating the air in the cavity to create a temperature gradient in the volume of air, the
temperature gradient having a first temperature at the first end and a second temperature at the
second end, the first temperature being lower than the second temperature; and
25 maintaining the temperature gradient for a predetermined time interval sufficient for
heating at least some of the plurality of hairs extending within the volume of air to a
temperature sufficient to remove at least part of at least some of the plurality of hairs, while
keeping the first temperature below the coagulation temperature of the region of skin.
- 30 44. A method for removing hairs from a region of skin, the region of skin having a plurality
of hairs, each of the plurality of hairs includes a first part disposed in a hair follicle within the
region of skin and a second part distal of the region of skin, the method comprising:
providing a cavity overlying the region of skin, the cavity comprising a volume of air
having a first end proximal to the region of skin and a second end distal to the region of skin;

heating the air in the cavity to create a temperature gradient in the volume of air, the temperature gradient having a first temperature at the first end and a second temperature at the second end, the first temperature being lower than the second temperature; and

5 maintaining the temperature gradient for a predetermined time interval sufficient for heating at least some of the plurality of hairs extending within the volume of air to a temperature sufficient to remove at least part of at least some of the plurality of hairs, while keeping the first temperature below the coagulation temperature of the region of skin.

10 45. A method according to claim 43 or claim 44 wherein the air cavity is a sealed air cavity.

46. A method according to any of claims 43-45 and including removing heat from the air after maintaining the temperature gradient, so as to keep the temperature of the skin below the coagulation temperature.

15 47. A method according to claim 46 wherein removing heat comprises, cooling the air in the cavity.

48. A method according to claim 47 wherein cooling the air comprises removing air from the cavity.

20 49. A method according to any of claims 42-48 wherein heating comprises providing a pulsed discharge.

50. A method according to any of claims 42-49 and including heating the skin and the first
25 part of the hair to a temperature below the coagulation temperature using electromagnetic radiation.

51. A method according to claim 50 wherein heating the skin and the first part of the hair includes filtering electromagnetic radiation to produce a pulse of non-coherent, narrow band
30 electromagnetic energy.

52. A method according to any of claims 42-51 heating comprises pulsing a flash lamp or an arc discharge lamp.

53. A method for removing hair by a person comprising:
applying heat from a portable hand held apparatus for hair removal, the apparatus comprising a housing having an opening, a switchable heat source disposed within the housing and a power source for energizing the heat source,
5 characterized in that the heat generates a temperature gradient in an air volume enclosed in a cavity formed by placing the opening on a region of skin, the temperature gradient being suitable for hair removal.
54. A method according to claim 53 wherein the applying of heat is performed by the
10 person on his own skin.
55. A method according to claim 53 or claim 54 further including manually removing the opening of the housing from the region of skin.
- 15 56. A method for hair removal by oneself comprising:
applying a heat pulse suitable for hair removal from a portable hand held apparatus, the applying performed by the person on his or her own skin.

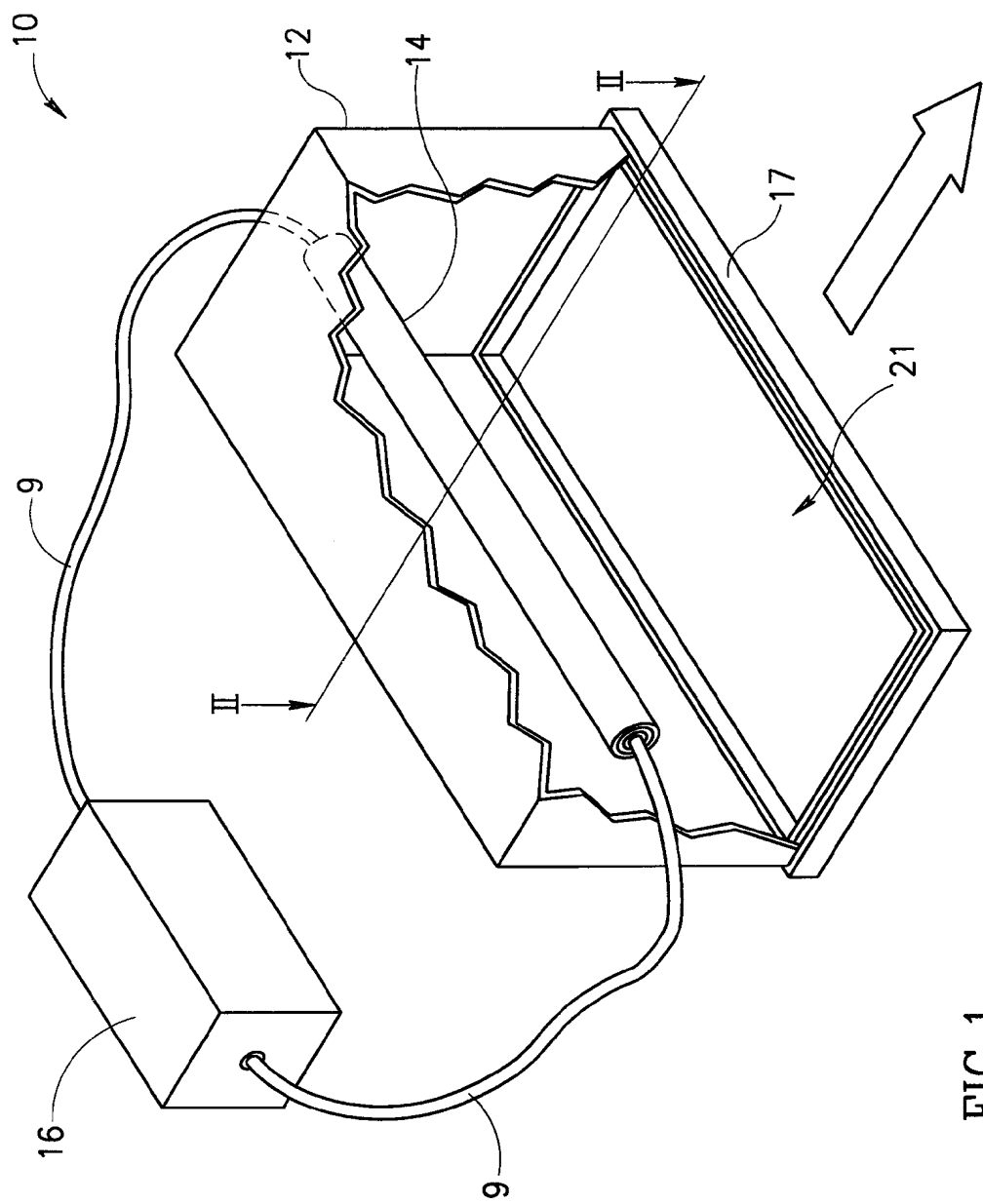
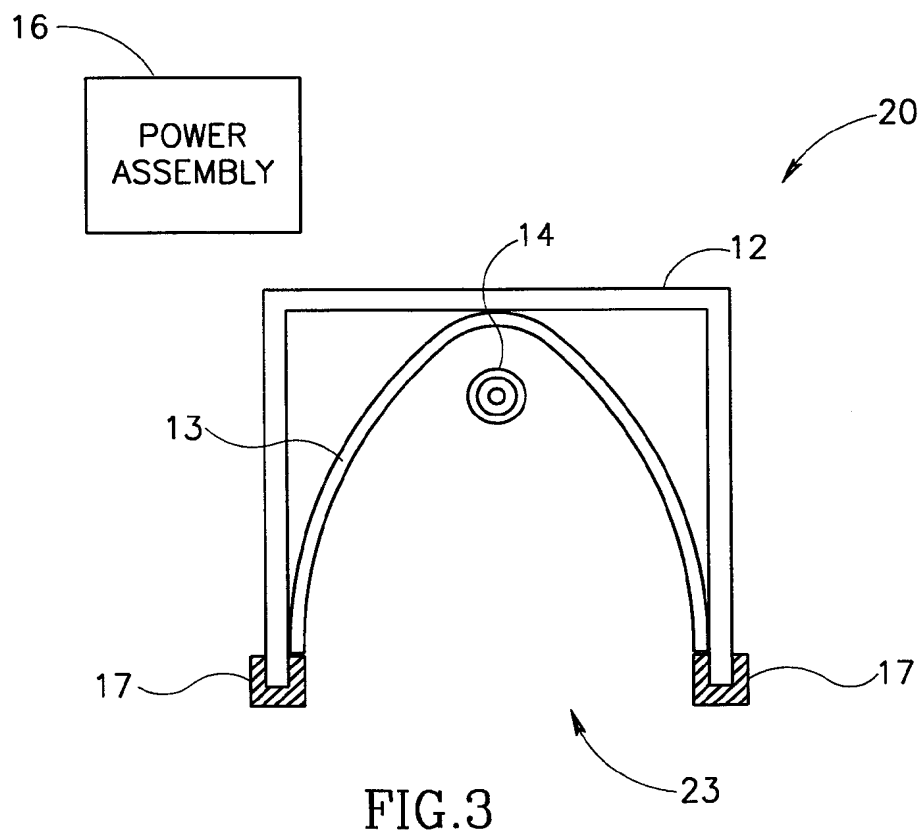
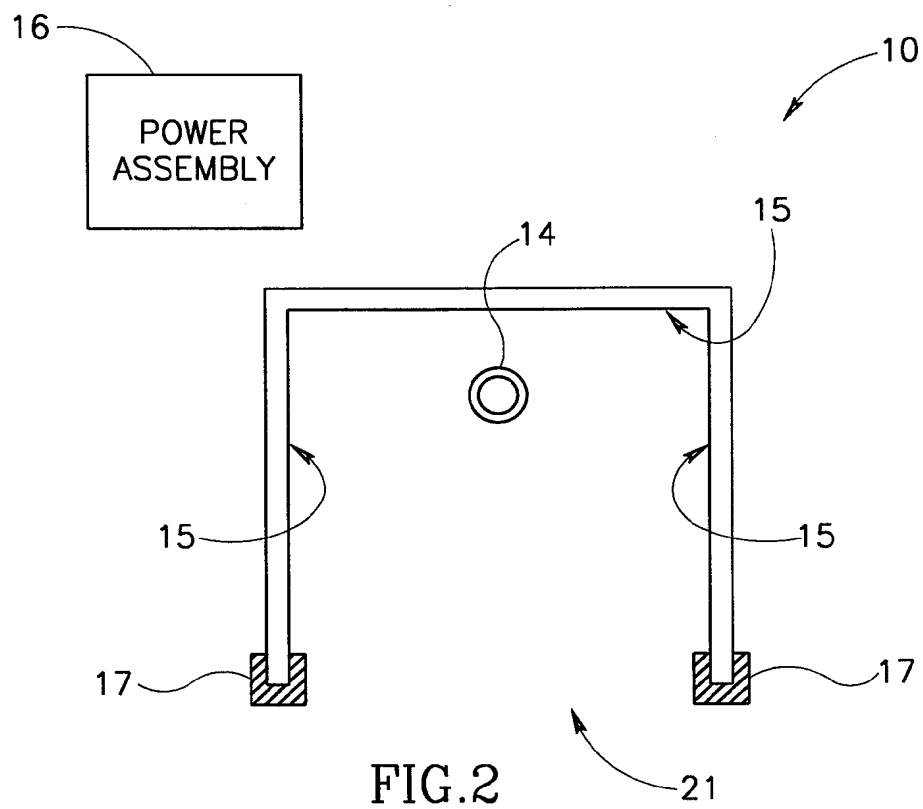


FIG. 1

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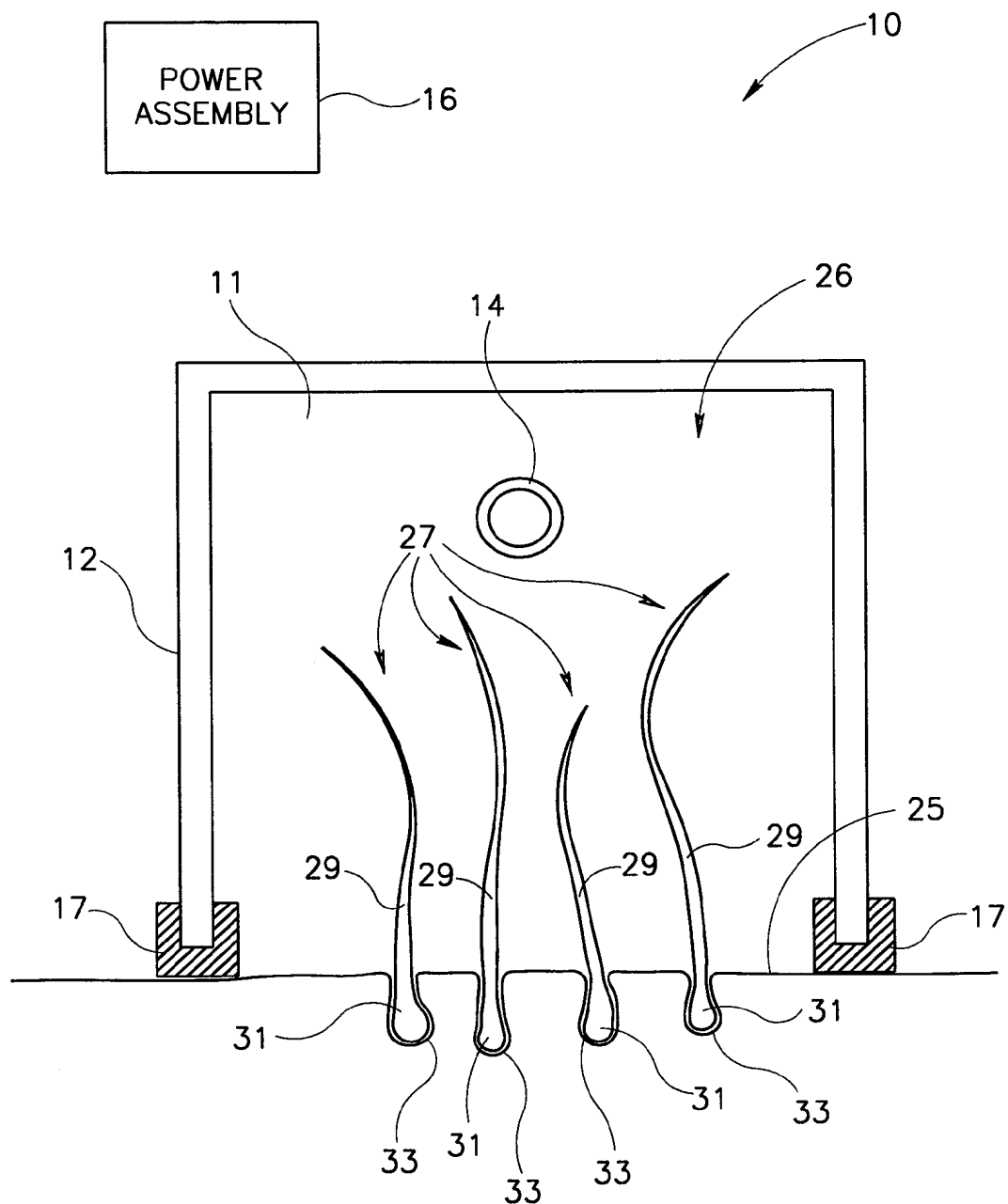


FIG.4

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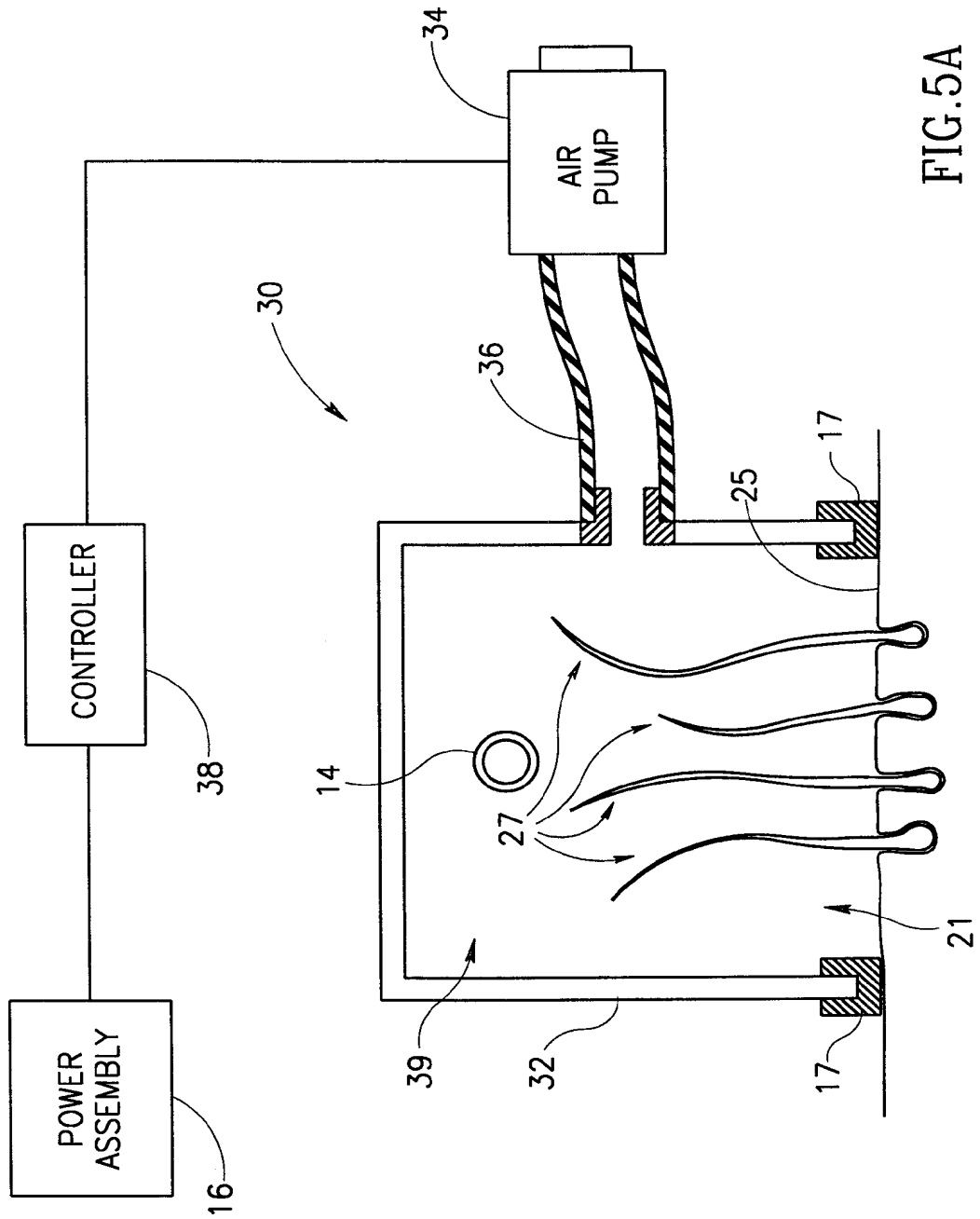


FIG.5A

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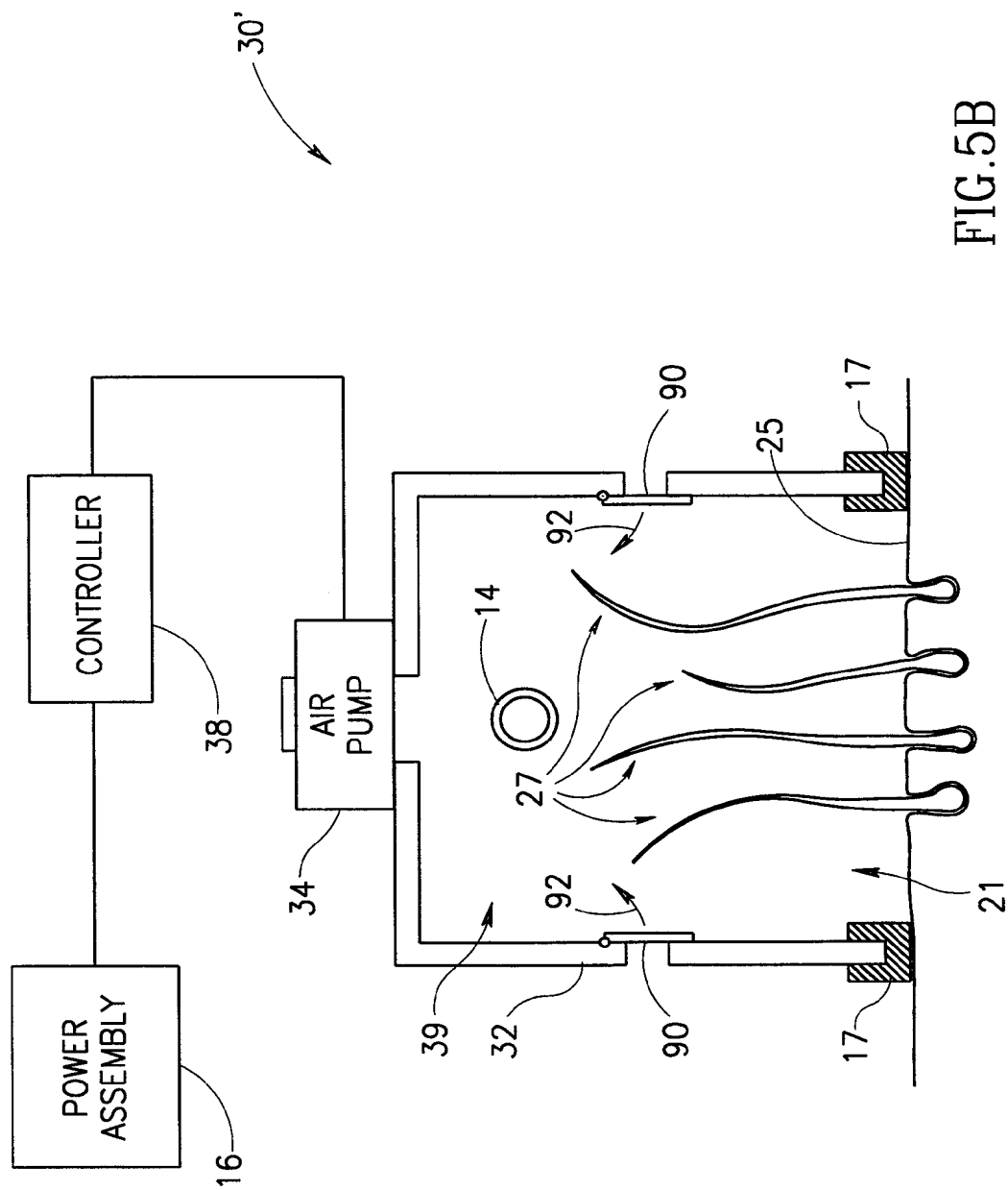
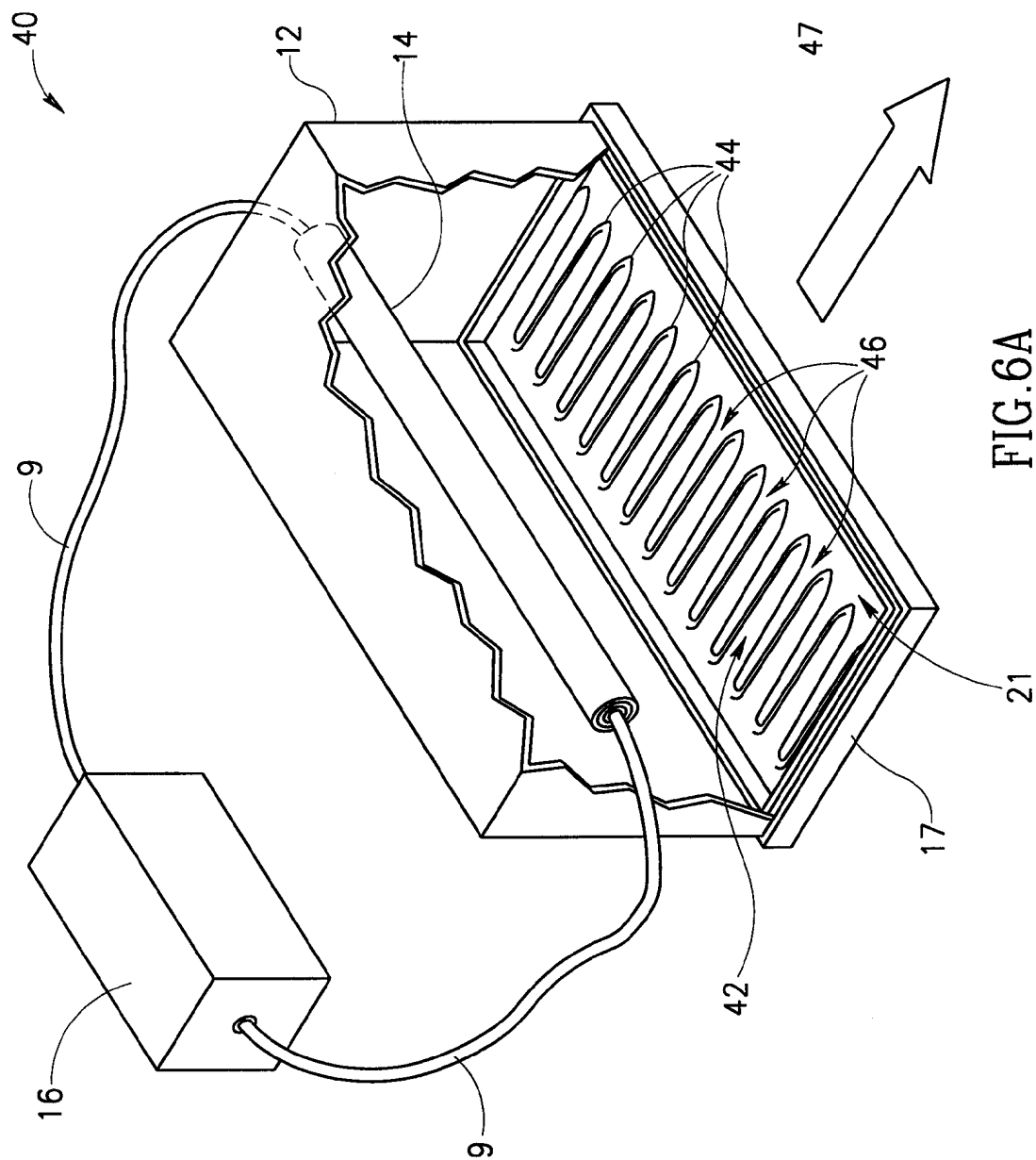


FIG.5B

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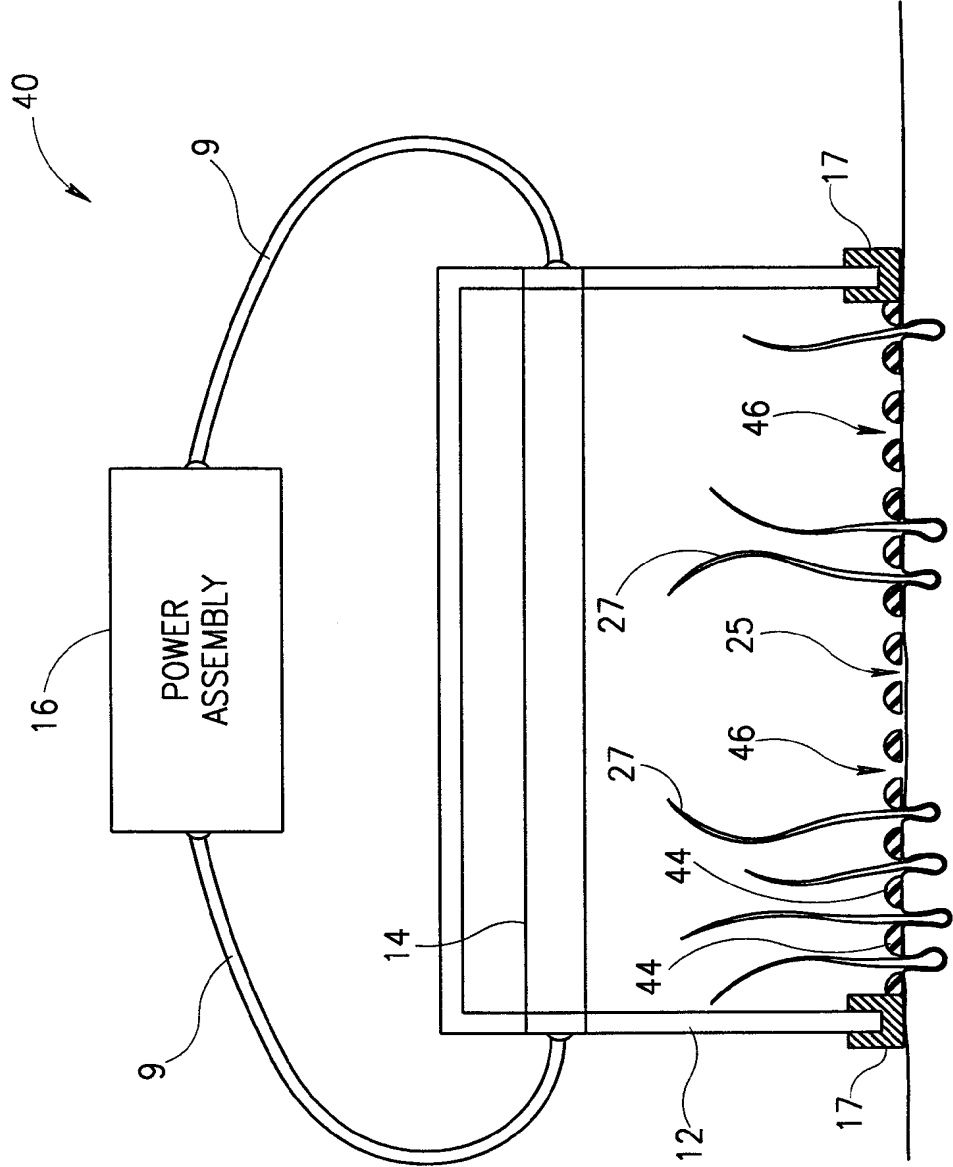
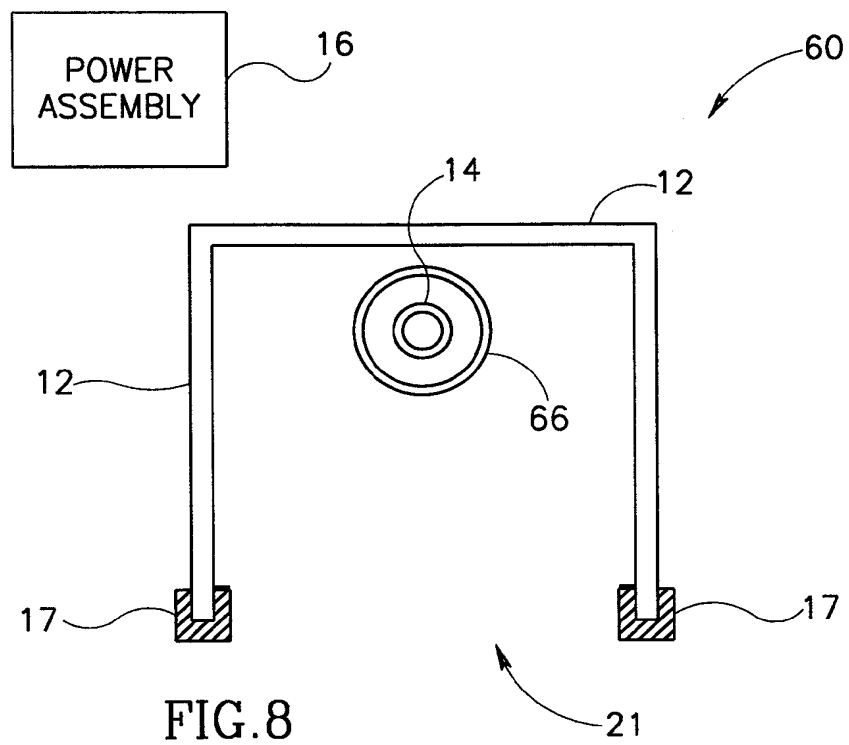
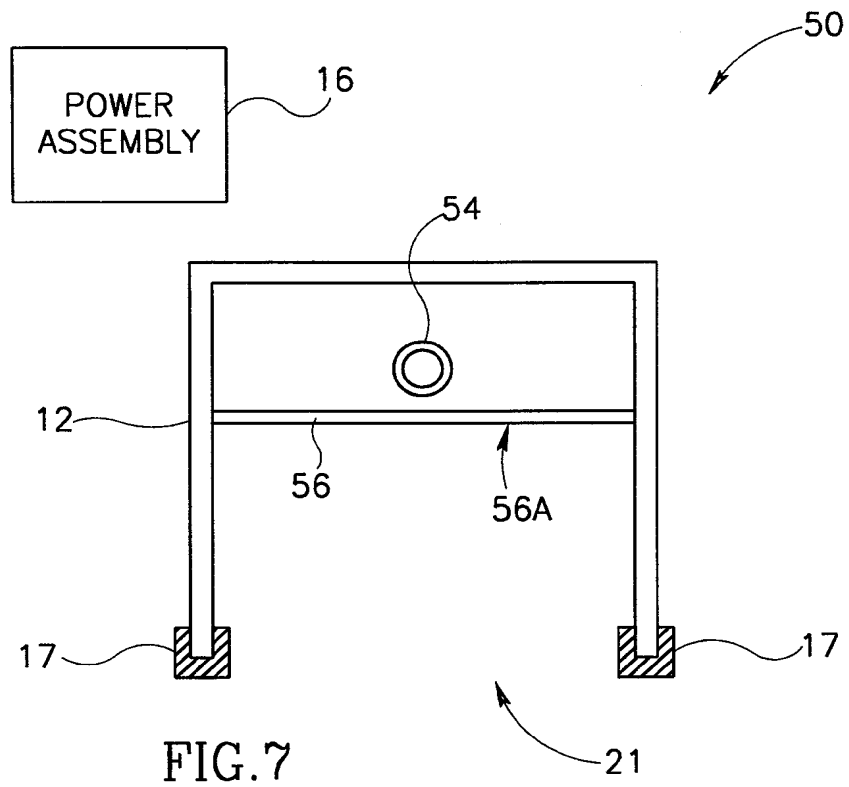


FIG.6B

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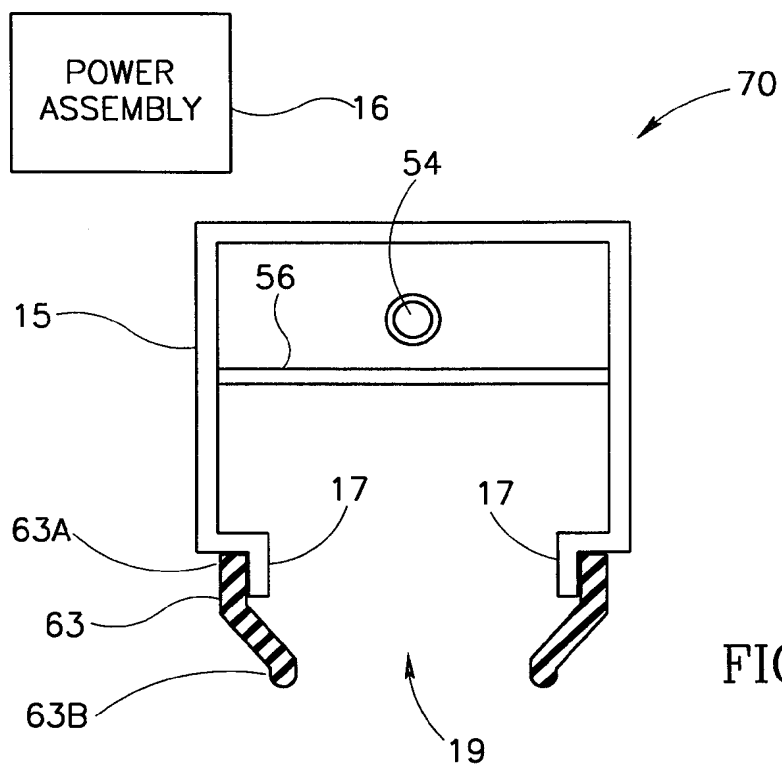


FIG. 9

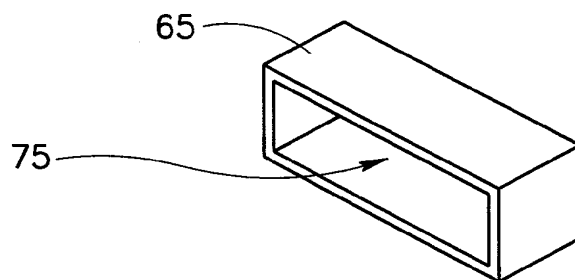


FIG. 10

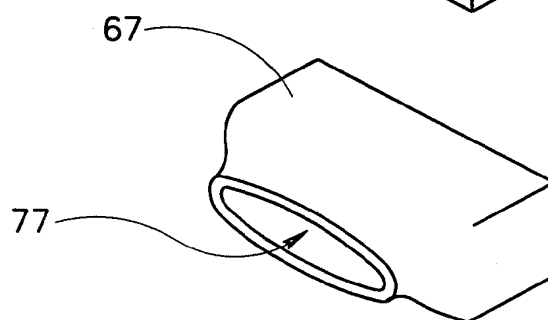


FIG. 11

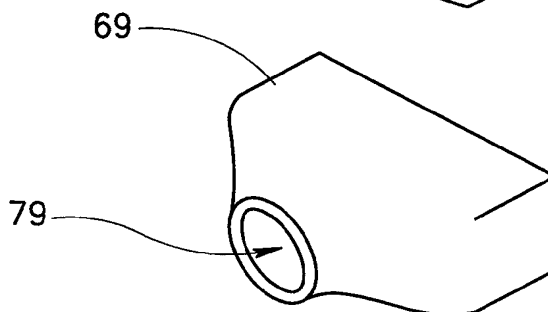


FIG. 12

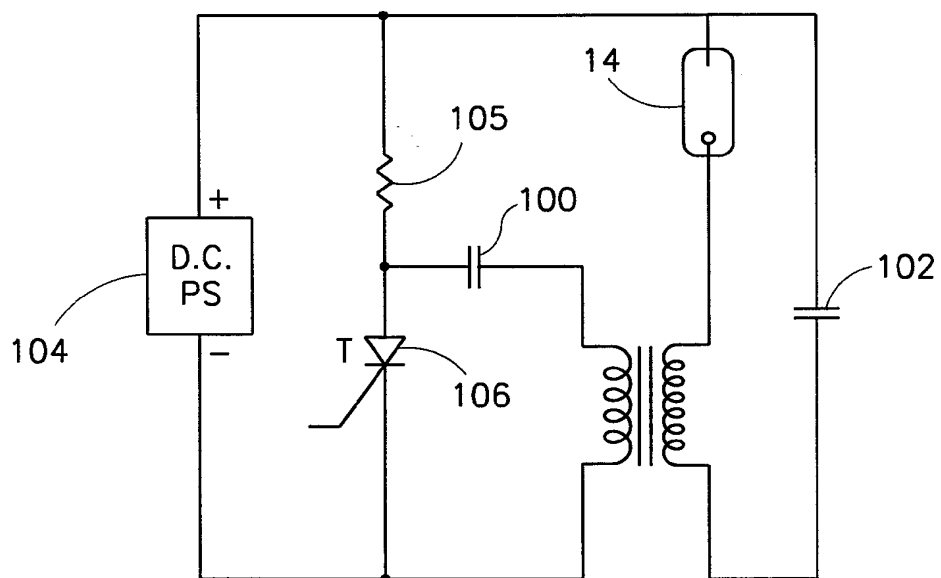
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FIG.13A

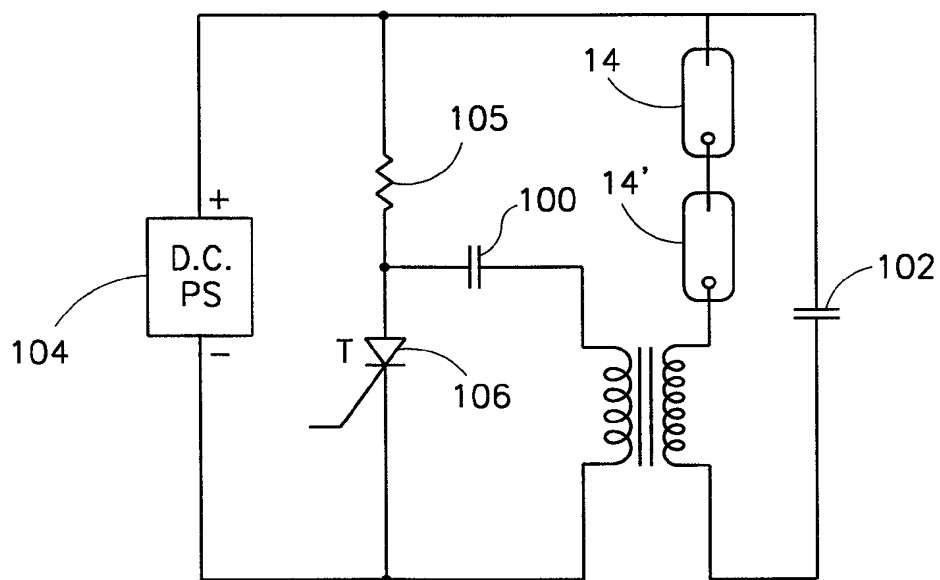


FIG.13B

INTERNATIONAL SEARCH REPORT

International Application No

PCT/IL 98/00605

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61N5/06 A45D26/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61N A45D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 3 934 115 A (PETERSON GERALD H) 20 January 1976 see column 1, line 48 - column 3, line 24; figures 1-4	1,2
X	EP 0 736 308 A (ESC MEDICAL SYSTEMS LTD) 9 October 1996 see column 1, line 3 - column 2, line 25 see column 6, line 52-54 see column 7, line 6-9 see column 8, line 13-21; figure 3	36,56
A		1-35, 37-55
A	US 5 595 568 A (FARINELLI WILLIAM ET AL) 21 January 1997 see the whole document	1-56



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

1 April 1999

Date of mailing of the international search report

15/04/1999

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Information on patent family members

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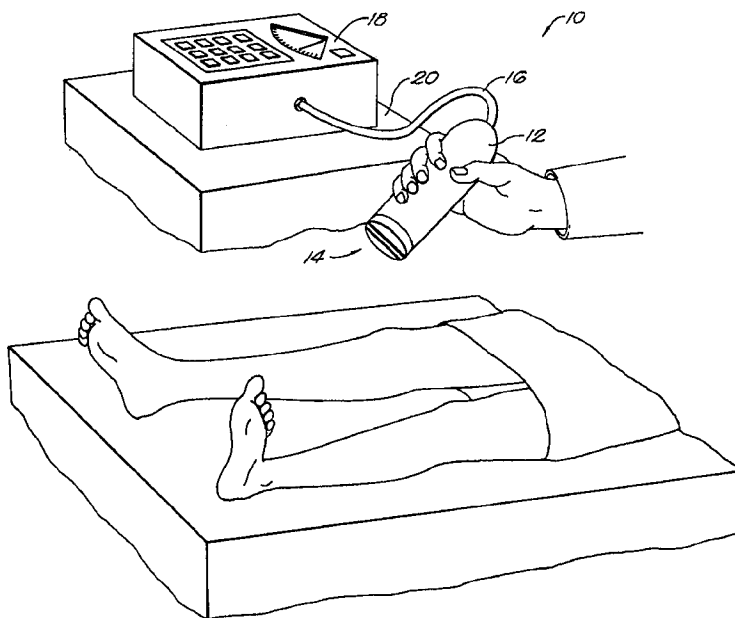
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(21) International Application Number: PCT/US99/02166 (22) International Filing Date: 2 February 1999 (02.02.99) (30) Priority Data: 09/017,968 3 February 1998 (03.02.98) US (71) Applicant: KIEFER CORP. [US/US]; 2 Arlington Road, Wellesley, MA 02181 (US). (72) Inventor: KLOPOTEK, Peter, J.; 2 Bayberry Lane, Framingham, MA 01701 (US). (74) Agents: ENGELLENER, Thomas, J. et al.; Nutter, McClen- nen & Fish, LLP, One International Place, Boston, MA 02110-2699 (US).		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>Without international search report and to be republished upon receipt of that report.</i>

(54) Title: HAIR FOLLICLE DEVITALIZATION BY INDUCED HEATING OF MAGNETICALLY SUSCEPTIBLE PARTICLES

**(57) Abstract**

Apparatus, methods, materials and systems for devitalizing hair follicles are disclosed in which magnetically susceptible particles are applied to a skin segment in a manner whereby the particles are deposited within the hair follicles and then subjected to a varying magnetic field to induce localized heating in the proximity of the particle, thereby devitalizing at least one component of the hair follicle to inhibit further hair growth.

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Hair Follicle Devitalization
By Induced Heating of Magnetically Susceptible Particles

Background of the Invention

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The technical field of this invention is the removal of hair and inhibition of hair regrowth by devitalization of certain hair structures within hair follicles.

15

Individual hair follicles comprise a bulb or cavity below the surface of the skin, from which a body of soft keratin is extruded. This shaft of keratin hardens as it passes through the bulb and ultimately protrudes from the skin surface as a "hair." A small cellular structure at the bottom of the cavity, the papilla, together with ancillary germinative structures, is responsible for the extrusion of the keratin which eventually forms into a hair. Permanent hair removal requires devitalization of the papilla or the structures that surround it.

20

The removal of body hair, a process commonly known as depilation, has been practiced with varying degrees of success for centuries by diverse methods and devices. For example, hot wax can be applied to a skin surface and allowed to harden around body hairs. Once the wax has hardened, it can be removed as a sheet, taking with it those hairs that have been entrapped by the wax. Typically, this is not a permanent process because the removal of the hair shaft does not prevent the regrowth of new hair from the shaft.

25

Various chemical depilatories have been used to remove hair. Typically these chemical agents are caustic, e.g., sodium hydroxide and the like, which makes the treatment process painful. Moreover, chemical depilatories are often not very effective.

30

Another approach to depilation is the use of electrical currents to destroy the delicate structures of the hair root. For example, U.S. Patent No. 5,049,148 issued to Mehl discloses an electrical device of this nature. Similar devices, generally known as "electrolysis" devices have been used in various forms, with and without the assistance of chemical adjuvants.

5 However, electrolysis is time consuming because the electrical current must be applied to each hair follicle individually.

10 An alternative approach for permanently impairing regrowth of many hair follicles at once is disclosed in U.S. Patent 5,470,332 issued to Mehl et al. which involves the application of a conductive material to the skin's surface and then applying an electric current to this conductive layer.

15 Most recently, a number of techniques for photocoagulation of the delicate hair structures by laser irradiation have been disclosed. For example, U.S. Patent No. 5595568 issued to Anderson et al., U.S. Patent No. 4,388,924 issued to Weissman, et al., and U.S. Patent No. 5,059,192 issued to Zaias disclose such laser irradiation techniques.

20 In addition, U.S. Patent 5,425,728 and U.S. Patent 5,226,907 issued to Tankovich disclose laser techniques in which the hair follicles on a section of skin are first contaminated with a substance (i.e. carbon particles) that has high absorption of light within a specific frequency band. The skin is then illuminated with such light, typically from a laser source, to heat the contaminating substance and kill the follicles or skin tissue feeding the hair root.

25 None of the processes described above are totally effective in depilating skin. There exists a need for better and more effective techniques. Accordingly, better methods and devices for hair removal would satisfy a long-felt need in the art.

Summary of the Invention

30 Apparatus, methods, materials and systems for devitalizing hair follicles are disclosed in which magnetically susceptible particles are applied to a skin segment in a manner whereby the particles are deposited within the hair follicles and then subjected to a varying magnetic field to induce localized heating in the proximity of the particle, thereby devitalizing at least one component of the hair follicle to inhibit further hair growth.

5 In one aspect of the invention, devices are disclosed which generate a time varying magnetic field and apply such field to a region of a patient's skin that has been treated with magnetically susceptible particles.

10 In one embodiment, the apparatus can include a source of alternating electric current that is applied to one or more coils surrounding at least a portion of a partially open ring-ferrite structure; the structure having an open gap adapted to engage a region of a subject's skin into the follicles of which magnetically susceptible particles have penetrated. Each electrically conductive coil structure is also electrically coupled to a capacitor, such that the coil and capacitance define a resonant circuit, whereby, upon
15 application of an electrical current to the coil, a magnetic field is formed in the gap which heats the magnetically susceptible particles within the hair follicle to induce depilation. The gap can range from about 1 millimeters to about 50 millimeters, more preferably from about 3 millimeters to about 15 millimeters.

20 Various other designs can be employed to deliver the time varying magnetic field to the target hair follicles. The ferrite structure need not be a simple ring but can take alternative geometric shapes designed to concentrate the magnetic field at the desired locus. A plurality of magnetic field guides can also be used. Alternatively, quasi-spherical emitters can be designed to create a similar magnetic field concentration.
25 In addition, ferrite structures can be replaced by other magnetic field guides or concentrators, such as magnetic metallic glasses and ferro-magnetic alloys. In some applications, a simple electromagnetic field generator alone can serve as a source and guide or concentrator to deliver a varying magnetic field to the desired area.

30 In an embodiment described in detail below, the field is generated by a resonant circuit to which a voltage is applied and a driver comprising one or more power transistors is employed to provide electronic impulses in synchrony with the frequency of the resonant circuit, thereby offsetting the energy dissipated by operation. The magnetic field guide (e.g., an open ferrite ring structure) can be readily incorporated
35 into a handpiece which permits the clinician to manually apply the magnetic field to the

5 treatment region. The open ring of ferrite is configured such that the gap is disposed at the tip of the handpiece in order to applied the magnetic field to the target tissue region. The handpiece can further include a coolant to extract the energy which is dissipated as heat with the field guide. The power source, driver electronics, a control
10 microprocessor, manual controls, coolant circulator and various other auxiliary systems can be housed in a remote structure to which the handpiece is connected by one or more cables providing electrical energy and/or coolant and any auxiliary functions to the handpiece.

15 In another aspect of the invention, methods are disclosed to induce hair depilation by magnetic-field heating of magnetically susceptible particles deposited within hair follicles. In one method, the hair shafts in a treatment region optionally can be first extracted by wax treatment and/or tweezers. (An anesthetic agent, such as Novocain can be applied before or after this step.) Optionally or alternatively, the skin can be cleaned to open the patient's pores. A slurry of magnetically-susceptible
20 particles is then applied to the treatment region in a manner that facilitates deposition of such particles in to the empty spaces of the hair follicles. Deposition into the follicles can be accomplished simply by manual rubbing, or with the aid of mechanical or pressurizing instruments. (For example, a vibrating applicator (e.g. an ultrasound applicator operating at about 10 – 20 kHz) can be used or a pressurized fluid (liquid or
25 gaseous) carrying such particles can be applied to a sealed region.)

Following application of the particles and deposition of such particles into the hair follicles, the skin surface can be cleaned of any excess particles or applicator fluid. The treated region is then ready for application of the alternating magnetic field. The
30 time-varying field induces localized heating of the particles, a portion of which will be located near enough to the papilla or other delicate structures to devitalize the hair follicle. It may also be desirable to heat the patient's skin (or monitor the skin temperature) to reduce the amount of energy that the particles need to deliver in order to kill the cells of the follicle.

5 The particles can then be removed (or left to be naturally cleared or metabolized
by the patient's body). The use of iron oxide particles is particularly advantageous
because such materials have very low toxicity and can be absorbed by the body and
used as nutrients. When removal is desired, mechanical suction, aided by vibration or
intermittent flushing (e.g., with water, saline or other solvents), can be employed.
10 Alternatively, magnetic forces can be applied to extract the magnetic particles.

 Such methods can further include the step of protecting any sensitive metallic
implants or prostheses before the application of the magnetic field. For example, dental
fillings or metal orthodontic braces may interfere with the removal of facial hair. Such
15 structures can be protected by one or more mouth guard-type insulators which are
fitted to surround any metallic dental work. The mouth guard is preferably flexible and
comprises a material that possesses high magnetic shielding properties. For example,
the mouth guard can be made from a plastic coated steel (or other metallic conductor).

20 In yet another aspect of the invention, compositions are disclosed for effecting
magnetic field heating of hair structures to induce depilation. The compositions include
magnetically susceptible particles having an average size sufficiently small to allow
penetration of at least a portion of said particles into the follicles on the target skin
segment and further having sufficient magnetic properties to induce localized heating in
25 the presence of variable magnetic field following penetration into the hair follicle to
devitalize at least one component of the hair follicle and thereby inhibit further hair
growth from within the follicle.

 The compositions can include a slurry of particles having an average particle
30 size ranging from about 5 Angstroms to about 100 micrometers in diameter, or more
preferably ranging from about 50 Angstroms to about 10 micrometers in diameter. The
compositions can further include particles of a lubricant material, such as surfactants, or
the particles can be coated with a lubricating material, such as a surfactant, or silicone,
hyaluronic compositions, dextran or combinations thereof. Such compositions can be
35 delivered to the skin as either dry slurries or as part of fluid delivery compositions.

5 Fluid delivery compositions according to invention can further include a fluid carrier that enhances penetration of the particles into the hair follicles. The fluid carriers can be lotions (e.g., aqueous or non-aqueous liquids or liquid solutions, as well as emulsions, suspensions) or gaseous mixtures. Liquid lotions can include surfactants, pore opening agents or transdermal penetrating enhancing agents. Gaseous carriers can include air or other gas mixtures, typically applied to the skin under pressure to drive the magnetically susceptible particles into the skin pores and, in particular, into the lower regions of the hair follicles. Gels or semi-solid materials, such as polyvinyl alcohols, which soften or liquefy under application pressure can also serve as a delivery medium for the particles.

15 In yet another aspect of the invention, systems or kits are disclosed for depilating hair, including compositions for effecting magnetic field heating of hair structures to induce hair depilation and one or more of the following components: topical anesthetics, wax compositions for hair extraction, apparatus for applying a variable magnetic field to a skin region, particle/lotion applicators, penetration enhancing devices, particle removal devices and protective shield structures.

25 The magnetic field generating apparatus can include a source of alternating electric current, a partially-open ring-ferrite structure; the structure having an open gap adapted to engage a region of a subject's skin and permitted an electrically conductive coil structure surrounding at least an portion of the ferrite structure and electrically coupled to the source of alternating current through a capacitance, such that the coil and capacitance define a resonant circuit, whereby, upon application of the compositions containing magnetically susceptible particles to hair follicles within the skin region and the application of an electrical current to the coil, a magnetic field is formed in the gap which heats the magnetically susceptible particles to induce depilation.

35 The terms "depilation" and "devitalization" as used herein are intended to encompass the devitalization of hair follicles, the destruction of hair papilla (and/or associated structures), inhibition of future hair growth, or interference with any portion of the normal hair cycle. The process of depilation as taught in the present invention

5 describes a variety of hair removal processes included, *inter alia*, the destruction (or substantial deactivation) of hair papilla and/or the epithelium columns that connect a growing or mature hair to the papilla; closure or modification of the hair follicle to preclude hair foliation; as well as simply the removal of the hair from the follicle. Such depilation or devitalization processes can be directed to single hair follicles or,
10 preferably to larger areas of skin to treat a region including more than one follicle, it being understood that depilation or devitalization over any region of skin may only be partially successful during an initial treatment according to the invention and a plurality of treatments may be necessary to obtain a desired result of general hair removal from a region of a subject's body.

15 The term "magnetically susceptible particles" as used herein is intended to encompass a wide range of either magnetic or electrically conductive materials, which are of a size that permits their passage into hair follicles. The magnetic or electrically conductive materials which can be used herein include any non-toxic metal, including
20 gold, silver and palladium, as well as magnetic metals such as iron, nickel and cobalt and their alloys, other conductive or magnetic metal alloys and metallic compounds which likewise possess electrical or magnetic properties. One such compound, magnetite, a magnetizable iron oxide having the general formula of Fe_3O_4 , has proved to be particularly useful in experimental trials, but various other materials may prove to
25 be more advantageous or useful for particular applications. The term "magnetically susceptible particles" encompasses not only materials that are inherently magnetically susceptible but also materials which become magnetically susceptible when deployed in the *in vivo* environment. The particles can be as small as individual molecules or ions. For example, spin transition polymers currently being developed for ultra dense
30 magnetic memory devices may be useful. On exemplary compound magnetically susceptible particles can have the general formula: $\text{Fe-R-I} \cdot n\text{H}_2\text{O}$, where R is atriazol, I is a cation or anion and $n\text{H}_2\text{O}$ is noncoordinated water.

35 Typically, the average size (i.e., the diameter or length of the longest dimension for non spherical shapes) of the magnetically susceptible particles can vary from about 5

5 Angstroms to about 100 micrometers, and more preferably from about 50 Angstroms
to about 10 micrometers. The magnetically susceptible particles can be applied to the
skin as a powder, in a liquid or as part of a lotion. Within a particular powder, liquid or
lotion the size of the particles can range by more than one, or even two, orders of
10 magnitude; the only critical factor being that a sufficient number of the magnetically
susceptible particles should be capable of entering the hair follicle cavity and lodging in
positions that facilitate depilation.

15 The term "magnetically-susceptible particles" is also used herein to encompass
coated particles as well as molecular structures that incorporate any of the above
referenced elements or compounds. Coating materials can include surfactants,
polysaccharides, such as dextran, as well as ficolls, silicones, chondroitin sulfates,
dextrane sulfates, laurates, inulins, and xylans. Molecular structures can include
ferritins, hemosiderins and similar materials which comprise a spherical protein cage in
which iron is stored (e.g., in the form of iron(III)oxyhydroxide). Colorants can also
20 form part of the particles.

25 A presently preferred embodiment comprises a coated magnetite powder. Such
powders are available from a variety of sources. For example, magnetite powders are
available from Ferrofluidics Corporation (Nashua, New Hampshire) and/or Toda
America Incorporated (Schaumburg, Illinois). As noted above, the average size of
individual magnetite particles can vary in size from about 10 angstroms to about 100
micrometers in diameter. The initial susceptibility of such particles ($4\pi M/H$) can range
from about 0.1 to 0.9 EMU/gauss/gFe.

30 It should be appreciated that the formula Fe_3O_4 for magnetite is an empirical
formula. Magnetite is more precisely described as a crystalline metal oxide having two
components: FeO and Fe_2O_3 . Two different valence iron ions occupy specific sites in
the crystal structure. The A metal is Fe^{+2} and the B metal is Fe^{+3} . The arrangement
causes a transfer of electrons between the different irons in a structured path or vector.
35 This electric vector generates the strong magnetic field associated with native magnetite

5 ores. Although magnetite is a presently preferred material for the magnetically susceptible particles of the present invention, various other materials may also be useful, including, for example, iron hydroxides, cobalt-Fe₃O₄, barium ferrites, and metallic iron particles.

10 Superparamagnetic particles (e.g. with initial susceptibilities greater than 0.5 EMU/gauss/gFe and/or negligible coercivity) can also be used. One such composition, a gamma ferric oxide, is disclosed in U.S. Patent 5,411,730 issued to Kirpotin et al on May 2, 1995 and incorporated herein by reference. This patent also describes various techniques for coating particles to form ferroliposomes and the like which can be
15 generally applicable to the present invention.

Colloidal suspensions of magnetite, coated with one or more surfactants, are also available from Ferrofluidics Corporation. More generally, suspensions of magnetically-susceptible particles can be formed with water, water/alcohol mixtures or
20 multiphasic liquids as the carrier. Suspensions useful in the present invention can vary in viscosity from about 1 centipoise to about 100,000 centipoise with magnetite concentration varying from about 0.5 volume percent to about 20 volume percent (yielding magnetic flux densities from about 20 gauss to about 1,000 gauss). One exemplary composition can be formed by coating magnetite particles with a cationic
25 surfactant and suspending such coated particles in a water/ethanol mixture. In other applications, anion, amphoteric or non-ionic surfactants may be preferred.

Lotions useful in the applying the magnetically susceptible particles to the skin can include aqueous and/or organic (e.g., oily or alcohol) fluids, as well as emulsions
30 having both aqueous and non-aqueous phases. The lotions are preferably chosen because of their ability to promote penetration of the magnetically susceptible particles into the cavities of the hair follicles. In some applications a proper balance of hydrophobic and hydrophilic components may be optimal in assisting penetration. In other applications the addition of an electrically charged component or the presence of
35 chemical additives with chemical moieties that present a surface electrical charge can be

5 useful. In yet other embodiments, it can be useful to employ lubricants such as silicones or hyaluronic compositions, either as coatings for the particles or as additional components of the lotion to enhance lubricity. Alternatively, chemical agents that induce expansion of the hair follicle openings can be useful.

10 Thus, the term "lotion" as used herein is intended to encompass solutions, such as aqueous and organic solvent solution and well as suspensions, emulsions and the like which serve as carriers for a magnetically susceptible particle or plurality of such particles. In one embodiment the lotion can be an aqueous solution including a surfactant. In another embodiment, the lotion can be a mixture of water and alcohol or
15 a mixture of water and aliphatic liquid. Alternatively, the lotion can be an oil alone or in conjunction with an emulsifying agent that ensures a uniform distribution of magnetically susceptible particles. The lotions can further include colorants, transdermal enhancing agents, as know in the art, and pore opening agents, likewise known in the art, to facilitate hair follicle penetration.

20 In the present invention, the application of the varying magnetic field to the magnetically susceptible particles induces rapid and extremely localized heating in the region of immediately surrounding the particles. Although no one theory of explanation may be entirely correct in analyzing this heating effect, it appears that the orientation
25 and reversal of domain polarities in magnetic materials as well as the creation of eddy currents in conductive materials both play a role in the superheating of the particles. When a particle is disposed within the hair follicle, the heat generated by the particle is sufficient to destroy or devitalized the follicle's internal structures necessary for hair growth.

30 "Alternating current" as used herein is intended to encompass not only sinusoidal waveforms, but also various other waveforms, such as pulsed, square wave, ramped, saw tooth, chirped waveforms and the like. The particular shape of the waveform is largely irrelevant so long as it can induce a variable magnetic field in the
35 target skin region where magnetically susceptible particles are heated to achieve the

5 desired depilatory effect on hair follicles. Similarly, the term "variable field" is intended
to encompass not only reversals of polarization but also pulsed fields and any other
magnetic field that changes over time in a manner that permits the transfer of energy
from the power supply to the magnetically-susceptible particles. The frequency of
alternation or variation can vary from about 1 kilohertz to about 10 gigahertz,
10 preferably from about 10 kilohertz to about 100 megahertz, and, in some applications,
it may be preferable to vary the frequency from about 20 kilohertz to about 20
megahertz or from about 50 kilohertz to about 3 megahertz.

15 Ferrite cores useful in channeling magnetic field lines can be obtained from
various sources including Magnetics, Inc. (Butler, PA); TDK Corporation (Tokyo,
Japan) or U.S. Philips Corporation (New York, New York). Ferrites useful in the
present invention encompass ferromagnetic compounds and iron-containing
compositions generally (including ferromagnetic alloys and magnetic metal glasses)
which exhibit high magnetic permeability and also high electrical resistivity. One
20 example of such materials is the 3F3 Ferrite manufactured by U.S. Philips Corporation.
The ferrite preferably is capable of generating a magnetic field of at least 0.02 Tesla
and, more preferably, a field greater than about 0.3 Tesla. In some applications a ferrite
core may not be necessary and instead can be replaced by an air coil (e.g. a torroidal
coil) or other arrangements that can serve as magnetic field guides.

25 The term "Curie temperature" or " T_c " as used herein is used as a measurement
of temperature (or temperature range) where magnetically susceptible materials
undergo a rapid change in their properties. For many of the magnetically susceptible
materials useful in the present invention it represents a plateau point beyond which
30 additional exposure to the variable magnetic field will not induce significant additional
heating effects. In applications where a lotion containing a substantial quantity of
magnetically susceptible particles is applied and penetrates into the skin, it is desirable
that the particles themselves exhibit a high enough Curie temperature to devitalize the
follicle by local heating effects but not induce significant thermal damage to
35 surrounding dermal structures. In some embodiments of the present invention, the

5 Curie temperature of the magnetically susceptible particles useful in the present invention is preferably greater than about 45°C, more preferably greater than about 60°C, and most preferably greater than about 75°C, but less than 600°C.

10 However, in other applications of the invention where the heating is very localized, the Curie temperature of the particles can be much greater, so long as the total application of depilating energy does not have significant adverse effects on surrounding tissue regions. Magnetite is an example of a very high Curie temperature material that is, nonetheless, particularly useful in certain applications of the invention.

15 The invention will next be described in connection with certain illustrated embodiments; However, it should be clear that various changes and modifications can be made by those skilled in the art without departing from the spirit and scope of the invention.

20 **Brief Description of the Drawings**

The invention may be more fully understood from the following description when read together with the accompanying drawings in which:

FIG. 1 is a schematic illustration of a system according to the invention for magnetic devitalization of hair follicles in a skin segment;

25 FIG. 2 is a more detailed cross-sectional schematic illustration of an apparatus for delivering a varying magnetic field according to the invention;

FIG. 3 is a schematic diagram of a driver circuit for the apparatus of FIG. 2;

30 FIGS 4A - 4E illustrate a method of hair follicle devitalization according to the invention; FIG 4A shows an optional initial step of removing hairs from a skin surface; FIG. 4B illustrates the application of magnetically susceptible particles to the skin surface; FIG 4C illustrates the migration of magnetically susceptible particles into the hair follicles and the removal of any excess magnetically susceptible particles and/or carrier fluid from the skin surface; FIG. 4D shows the application of a varying magnetic field to induce heating of the particles; and FIG. 4E illustrates the optional further step of removing the particles from the follicles following treatment;

35 FIG. 5 illustrates an apparatus for applying magnetically susceptible particles to follicles in a skin segment;

5 FIG. 6 illustrates an alternative apparatus for applying magnetically susceptible particles to follicles in a skin segment;

 FIG. 7 illustrates another alternative apparatus for applying magnetically susceptible particles to follicles in a skin segment;

10 FIG. 8 illustrates an apparatus for removing magnetically susceptible particles from follicles in a skin segment;

 FIG. 9 illustrates an alternative apparatus for removing magnetically susceptible particles from follicles in a skin segment; and

 FIG. 10 illustrates a protective cover for dental work when removal of facial hair is desired.

15 Detailed Description

 In FIG. 1, a system 10 for magnetic follicle devitalization is shown comprising a handpiece 12 which houses a magnetic field generating open-ring ferrite structure. The open-ring is oriented such that the opening in the ring forms a gap 14 at the distal end of handpiece 12. The handpiece is connected via conduit 16 to a controller 18 and an auxiliary housing 20 (which can include driver electronics, a control microprocessor, manual controls, a coolant circulator and various other auxiliary systems).

25 In FIG. 2, the handpiece 12 of FIG. 1 is shown in more detail including the ferrite ring structure 30, an inductive coil 32 which is wrapped around the ferrite core and a capacitor and/or other electronics 35. Power to generate a magnetic field within the ferrite 30 can be supplied from the housing 20 (shown in FIG. 1) via electrical cables 40. The handpiece can also incorporate an internal cooling chamber 34 which is supplied with coolant via a coolant source conduit 36. The coolant circulates within the chamber 34 to extract heat which otherwise would build up in the ferrite ring 30. Heated coolant can be withdrawn from the handpiece via a coolant exit conduit 38 for recycling within the housing or disposal. The electrical cables as well as the coolant supply and extraction conduits can all be encased within a single tubing 16 (or, alternatively, separate cables can be employed for electrical power and coolant delivery). The shell 28 or rim 29 of the handpiece 12 can also be used to heat the patient's skin. The rim 29 can also include a marker mechanism (e.g., an ink application) 27 which serves to delineate areas which have been treated.

5 The electronic circuitry 35 within the instrument (in cooperation, if necessary, with an auxiliary processor within housing 20) can also include an electronic sensor for metallic implants such as dental work (e.g., metallic fillings and/or orthodontic braces) that may need to be protected if the treatment region is in close proximity to such an implant.

10 In FIG. 3, an electrical schematic diagram of a driver circuit for the magnetic field-generating ferrite ring 30 is shown comprising the inductive coil labeled " L_1 " in the drawing. As shown, it consists of 6 turns of wire about the ferrite torroid 30 (shown in phantom). The inductor L_1 is connected to capacitor C, as shown, and supplied with a
15 current via a center tap. Power transistors T_1 and T_2 serve to inject additional energy into the circuit as energy is lost (as heat) in the ferrite core 30 and/or other components of the circuit. In one illustrative embodiment, about 2 amperes is supplied via choke L_2 to the center tap. The choke L_2 can have an inductance of 350 microhenries and the 6 turn inductor L_1 can have an inductance of about 3.5 microhenries. The capacitor C can
20 have a capacitance of about 0.08 microfarads. Power transistors T_1 and T_2 are N-channel MOSFET transistors (Model No. IRFP460LP) available from the International Rectifier Corporation.

25 Together the inductance L_1 and the capacitors C form a resonant circuit with approximately 70 amperes of current flowing back and forth. Preferably, the resonant circuit of the coil L_1 and capacitance C has a Q factor over 10. The opening and closing of transistors T_1 and T_2 are timed to synchronize with the resonant frequency of the LC circuit. The ferrite core can be a open-toroidal structure (with a gap of about 7 mm) made, for example, from 3F3 ferrite material available from the U.S. Phillips Corporation.
30 This current-fed resonant push-pull circuit serves to generate an oscillating magnetic field within the ferrite ring 30 (and across the gap) at the same frequency as the resonant LC circuit.

35 All matter exhibits magnetic properties when placed in an external magnetic field. Even non-magnetic metals, such as copper and aluminum, are affected by the presence of a magnetic field. Materials that are attracted to the pole of a magnet are classified as paramagnetic, while those that are repulsed are classified as diamagnetic. Materials, such as iron, that exhibit a very strong attraction towards the pole of a magnet are further classified as ferromagnetic. Whether a substance is paramagnetic or diamagnetic depends

5 primarily on the presence or absence of free magnetic dipole moments in the material's constituent atoms.

10 Because paramagnetic materials have free magnetic dipole moments, the presence of a magnetic field will induce alignment of the normally randomly aligned moments (or domains) of the material. When an alternating magnetic field is applied to such materials, the dipoles will attempt to reverse their orientation. As the dipoles are cycled back and forth, heating occurs at the microscopic level until a certain temperature (dependent on the material) is reached. This temperature is typically referred to as the Curie temperature and represent a plateau for many materials at which they exhibit minimal responses to further magnetic excitation.

15 In one embodiment the present invention can take advantage of this property of magnetically susceptible materials by "tuning" the frequency and duration of the varying magnetic field to ensure that the magnetically susceptible particles are rapidly brought to their Curie temperature and held there only for a period of time sufficient to induce apoptosis of the hair papilla and/or other hair structures.

20 In another embodiment of the invention, heat is generated by interaction between the magnetically susceptible particle and a fluid carrier. When such a magnetically susceptible particle is exposed to an alternating or rotating magnetic field while it is in a fluid, the particle will be induced to rotate or swing into alignment with the field. The mechanical friction between the particle and the fluid dissipates the field energy as heat in fluid surrounding the particle. The optimal frequency for heating will depend upon the particle's magnetic movement, its moment of (rotational) inertia and, to some extent, the viscosity of the surrounding fluid. At frequencies above the optimal frequency (for a particular particle and fluid composition) the moment of inertia for individual particles will inhibit heating because the particles will be unable to swing in response to such high frequencies.

25 30 35 FIGS. 4A-4E illustrate a method of hair follicle devitalization according to the invention. In FIG. 4A, hair shafts 41 are removed from the lumens or cavities 42 of hair follicles. The hair shafts 41 can be removed, for example, by the application of a hot liquid wax 44 and, after solidification, removal of the wax 44 from the patient's

5 skin. Alternatively, tweezers or other mechanical instruments can be employed to remove hair shafts from the treatment site.

10 In FIG. 4B, a slurry or lotion 45 containing magnetically susceptible particles 46 is applied to the surface of the skin 47. Following application, a portion of the slurry or lotion (and the magnetically susceptible particles) penetrate into the individual hair follicles as shown in FIG. 4C. Once penetration is achieved, the excess slurry or lotion can be removed from the patient's skin surface 47.

15 In FIG. 4D, the magnetic field generating apparatus of the present invention is applied to the skin. As illustrated, a ferrite ring structure 30 (shown in phantom) is pressed against the skin causing a slight indentation and squeezing the treatment area into the gap region 48 such that the magnetically susceptible particles 46 are subjected to the magnetic field 48. (It should be appreciated that the magnetic field generator can engage the skin without direct contact. In some embodiments, engagement can be
20 achieved by simply aiming the magnetic field generator at the target skin region. The term "engage" as used herein is intended to encompass both physical contact and non-contact relationships -- in which the magnetic field is applied by an instrument at some distance from the treatment area.) The alternating current of the applicator causes an varying magnetic field in the gap region 48 and induces localized heating of particles
25 46. One or more particles disposed within the cavity of the follicle is sufficient to devitalize it by heating effects, as shown in FIG. 4D.

30 In FIG. 4E the magnetically susceptible particles 46 can be removed with a removal apparatus 49, employing either suction or magnetic forces to dislodge and detract the magnetic particles following treatment, as shown in FIG. 4E.

In FIG. 5, a applicator structure 50 is shown comprising a hand-held housing 52 and a source 58 of magnetically susceptible particles 46. Particles can be driven into the skin by pressure. The air or fluid pressure supplied by instrument 50 causes at least

5 a portion of the magnetically susceptible particles to penetrate into the cavities 42 of the hair follicles. A sealing rim 59 can also be incorporated.

10 In FIG. 6, an alternative applicator 50A is shown which includes a vibrating rim 62. The instrument 50A not only can apply air or fluid pressure to induce particle penetration but the vibration of rim element 62 further enhances the penetration of the magnetically susceptible particles 46 into the cavities 42.

15 In FIG. 7 yet another applicator 50B is shown in the form of a hand held reservoir 63 for magnetic particles 46 in a polymeric matrix 65. The applicator 50B can be similar in form and composition to deodorant sticks and employ a semi-solid or gel carrier (such as a polyvinyl alcohol) which changes viscosity upon application of pressure to release the particles into the follicle cavities.

20 In FIG. 8, a particle extraction device 70 is shown which employs a rim gasket (or oscillating ring element) 72 to isolate the region from which the magnetic particles will be extracted following therapy. The lumen of the instrument 70 can be connected to pump 76 supply suction or, alternatively, a combination of flushing and suction to facilitate particle removal.

25 In FIG. 9, yet another embodiment of a removal apparatus 80 is shown including not only a suction function but also a magnet 86 which can be either a permanent or oscillating electromagnet which further assists in the removal of the magnetically susceptible particles by magnetic attraction. This magnetic attraction function can, of course, be combined with either suction or flushing and/or mechanical
30 vibration of the skin to cooperate in the removal of the particles 46.

35 In FIG. 10 another auxiliary component of the invention, a protective covering 90 is shown. This protective covering 90 is specifically adapted to protect a patient's dental work (e.g., metallic fillings and/or orthodontic braces) during the removal of facial hair. The instrument 90 is shaped in the form of a mouth guard and has a curved

5 groove into which a patient's teeth can be inserted. (Although a single mouth guard for
an upper set of teeth is shown in FIG. 9, it should be clear that similar devices can also
be employed for protection of the patient's lower set of teeth and other forms can be
used to protect other portions of the patient's body.) Preferably, the instrument 90 is
made of a malleable plastic material and is filled internally with a substance (e.g., a
10 metal or other electrically conductive material) that effectively shields the teeth from
magnetic fields.

5

Claims

1. An apparatus for devitalizing hair follicles, comprising:
a magnetic field guide adapted to engage a region of skin; and
a generator for producing a varying magnetic field and applying the
varying field to the skin through the field guide,
whereby, upon application of magnetically susceptible particles to hair
follicles within the skin and generation of the varying magnetic field, the particles are
heated to devitalize the hair follicles.

10

2. The apparatus of claim 1 wherein the varying magnetic field has a
frequency ranging from about 1 kilohertz to about 10 gigahertz.

15

3. The apparatus of claim 1 wherein the varying magnetic field has a
frequency ranging from about 10 kilohertz to about 100 megahertz.

20

4. The apparatus of claim 1 wherein the varying magnetic field has a
frequency ranging from about 20 kilohertz to about 20 megahertz.

5. The apparatus of claim 1 wherein the varying magnetic field has a
frequency ranging from about 50 kilohertz to about 3 megahertz.

25

6. The apparatus of claim 1 wherein the apparatus further comprises
source of alternating electric current;
a magnetic field guide having an open gap adapted to engage a region of
a subject's skin

30

an electrically conductive coil structure surrounding at least an portion
of the magnetic field guide and electrically coupled to the source of alternating current
through a capacitance, such that the coil and capacitance define a resonant circuit,

whereby, upon application of magnetically susceptible particles to hair
follicles within the skin region and the generation of an electrical current in the coil, a

35

5 varying magnetic field is formed in the gap which heats the magnetically susceptible particles to induce depilation.

10 7. The apparatus of claim 6 wherein the magnetic field guide comprises a ferrite structure.

15 8. The apparatus of claim 6 wherein the ferrite structure comprises an iron-containing composition.

20 9. The apparatus of claim 6 wherein the ferrite structure upon application upon an electric current to the coil, the apparatus generates a varying magnetic field having a peak strength of at least 0.02 Tesla in the gap.

25 10. The apparatus of claim 6 wherein the ferrite structure upon application upon an electric current to the coil generates an magnetic field of at least 0.3 Tesla in the gap.

30 11. The apparatus of claim 6 wherein the gap in the ferrite structure is less than 50 millimeters.

35 12. The apparatus of claim 6 wherein the gap in the ferrite structure is adapted to pinch and hold a region of skin during treatment.

40 13. The apparatus of claim 6 wherein the resonant circuit of the coil and capacitance has a Q factor over 10.

45 14. The apparatus of claim 6 wherein the resonant circuit further comprises a power supply of at least 100 watts.

5 15. The apparatus of claim 6 wherein the apparatus further comprises a driver circuit in synchrony with the resonant circuit to inject additional energy into the resonant circuit to compensate for energy losses.

10 16. The apparatus of claim 15 in which the driver circuit further includes at least power transistor which is switched on and off in synchrony with the frequency of resonant circuit.

15 17. The apparatus of claim 1 wherein the apparatus further comprises a coolant chamber which extracts excess heat from the apparatus during use.

 18. The apparatus of claim 1 wherein the apparatus further comprises a shield which reduces electric field effects on the skin region.

20 19. The apparatus of claim 1 wherein the apparatus further comprises a heater element for heating the skin region.

 20. The apparatus of claim 1 where in the apparatus further comprises a handpiece which houses the magnetic field guide.

25 21. A method of devitalizing a hair follicle on a skin segment, comprising, applying magnetically susceptible particles to the skin segment in a manner whereby at least one magnetically susceptible particle is deposited within a hair follicle; subjecting said deposited particle to a varying magnetic field to induce localized heating in the proximity of the particle such that said heat devitalizes the hair follicle to
30 inhibit further hair growth.

 22. The method of claim 21 wherein the method further comprises applying a slurry containing said magnetically susceptible particles to the skin segment such that penetration of the hair follicle occurs by infiltration.

5 23 The method of claim 21 wherein the magnetically susceptible particles are applied to the skin segment by applying a lotion containing magnetically susceptible particles onto the skin segment.

10 24. The method of claim 21 wherein the method further comprises initially removing the hair shafts from the follicles so that the cavities of the hair follicles are exposed.

15 25. The method of claim 24 wherein the step of removing the hair shafts further comprises applying a wax to the skin and then removing the wax with the hair shafts entrained therewith.

20 26. The method of claim 21 wherein the method further comprises applying a chemical hair defoliant agent prior in order to remove at least some the hair shafts prior to applying the magnetically susceptible particles.

 27. The method of claim 21 wherein the method further comprises applying a dermal pore-opening agent in order to enlarge the openings of the follicle cavities prior to applying the magnetically susceptible particles.

25 28. The method of claim 21 wherein the method further comprises applying a cleaning agent prior to applying the magnetically susceptible particles.

 29. The method of claim 21 wherein the method further comprises applying a degreasing agent prior to applying the magnetically susceptible particles.

30 30. The method of claim 21 wherein the method further comprises drying the skin segment prior to applying the magnetically susceptible particles.

35 31. The method of claim 21 wherein the method further comprises applying a vibrational force, such as ultrasound at a frequency of about 10kHz to about 20 kHz,

5 to the skin segment to enhance the penetration of magnetically susceptible particles into the hair follicles.

32. The method of claim 21 wherein the method further comprises applying
a fluid pressure to the skin segment to enhance the penetration of magnetically
10 susceptible particles into the hair follicles.

33. The method of claim 21 wherein the method further comprises applying
a magnetic field to the skin segment to enhance the penetration of magnetically
susceptible particles into the hair follicles.

34. The method of claim 21 wherein the method further comprises marking
the skin segment following treatment.

35. An apparatus for devitalizing hair follicles, comprising:
means for guiding a magnetic field and for engaging a region of skin; and
means for producing a varying magnetic field and applying the varying
field to the skin through the field guide,
whereby, upon application of magnetically susceptible particles to hair
follicles within the skin and generation of the varying magnetic field, the particles
25 devitalize the hair follicles.

36. The apparatus of claim 35 wherein the apparatus further comprises
means for marking a treated region following treatment.

37. The apparatus of claim 35 wherein the apparatus further comprises
means for sensing the proximity of conductive implants that could be adversely affected
by a varying magnetic field.

38. The apparatus of claim 35 wherein the means for producing a time-
varying magnetic field is a resonant circuit.

5 39. The apparatus of claim 35 wherein the field guide means is a ferrite structure.

 40. An apparatus for depilating hair, comprising
 means for generating an alternating electric current;
10 means for guiding a magnetic field and for engaging a region of a subject's skin
 an electrically conductive coil structure surrounding at least an portion
of the field guide means and electrically coupled to the source of alternating current
through a capacitance, such that the coil and capacitance define a resonant circuit,
15 whereby, upon application of magnetically susceptible particles to hair
follicles within the skin region and the generation of an electrical current in the coil, a
varying magnetic field is formed in the gap which heats the magnetically susceptible
particles to induce depilation.

20 41. A composition for depilating hairs growing on a skin segment,
comprising a plurality of magnetically susceptible particles having an average size
sufficient small to allow penetration of at least a portion of said particles into hair shafts
on said skin segment and further having sufficient magnetic properties to induce
localized heating in the presence of variable magnetic field following penetration of a
25 hair follicle to devitalize at least one component of the hair follicle and thereby inhibit
further hair growth from with said shaft.

 42. The composition of claim 41 wherein the particles have an average
particle size ranging from about 5 Angstroms to about 100 micrometers in diameter.

30 43. The composition of claim 42 wherein the particles have an average
particle size ranging from about 50 Angstroms to about 10 micrometers in diameter.

35 44. The composition of claim 41 wherein the composition further comprises
a lubricant material.

5 45. The composition of claim 44 where the lubricant material is selected
from the group consisting of water, alcohols, aliphatic liquids and surfactants and
combinations thereof.

10 46. The composition of claim 41 wherein the particles are coated with a
lubricating material.

15 47. The composition of claim 46 where the lubricant coating material is
selected from the group consisting of silicones, hyaluronic compositions,
polysaccharides and combinations thereof.

 48. The composition of claim 41 wherein the particles are a dry slurry.

20 49. The composition of claim 41 wherein the composition further comprises
a particle delivery medium that enhances penetration of the particles into the hair shafts.

 50. The composition of claim 41 wherein the particle delivery medium is
selected from the group of air, water, alcohols, oils, emulsions, and combinations
thereof.

25 51. The composition of claim 41 wherein the particle delivery medium
further comprises a semi-solid material that changes viscosity under pressure.

 52. The composition of claim 51 wherein the semi-solid material comprises
a polyvinyl alcohol.

30 53. The composition of claim 41 wherein the particle delivery medium
further comprises a germicidal agent.

35 54. The composition of claim 41 wherein the particle delivery medium
further comprises an electrically charged moiety.

5 55. The composition of claim 41 wherein the particle delivery medium
further comprises a material having low surface tension.

 56. The composition of claim 41 wherein the composition further comprises
an anesthetic agent.

10 57. The composition of claim 41 wherein the composition further comprises
a pore penetration enhancing agent

 58. The composition of claim 41 wherein the particles further comprises a
15 paramagnetic material.

 59. The composition of claim 41 wherein the particles further comprises a
iron containing material.

20 60. The composition of claim 41 wherein the particles further comprises
magnetite.

 61. The composition of claim 41 wherein the particles further comprise a
material having a Curie temperature of at least 45 degrees C.

25 62. The composition of claim 41 wherein the particles further comprise a
material Having an initial susceptibility of at least 0.1 EMU/gauss/gFe.

 63. The composition of claim 41 wherein the particles further comprise a
30 material having an initial susceptibility of at least 0.3 EMU/gauss/gFe.

 64. The composition of claim 41 wherein the composition further comprises
a colloidal suspension of magnetite, iron or cobalt or alloys or compounds containing
such materials.

35

5 65. The composition of claim 64 wherein the particles are coated with a
surfactant.

 66. The composition of claim 41 wherein the particles are coated with an
acid surfactant.

10 67. The composition of claim 41 wherein the particles are coated with an
electrically charged surfactant.

 68. The composition of claim 41 wherein the particles are coated with a
15 cationic surfactant.

 69. The composition of claim 41 wherein the particles are coated with an
anionic surfactant.

20 70. The composition of claim 41 wherein the particles are coated with a
amphoteric surfactant.

 71. An kit for depilating hair, comprising
 a magnetic field guide adapted to engage a region of skin; and
25 a generator for producing a varying magnetic field and applying the
varying field to the skin through the field guide,
 whereby, upon application of magnetically susceptible particles to hair
follicles within the skin and generation of the varying magnetic field, the particles
devitalize the hair follicles.

30 72. The kit of claim 71 wherein the kit further comprises a supply of
magnetically susceptible particles.

 73. The kit of claim 71 wherein the kit further comprises an applicator for
35 applying magnetically susceptible particles to a skin region.

5

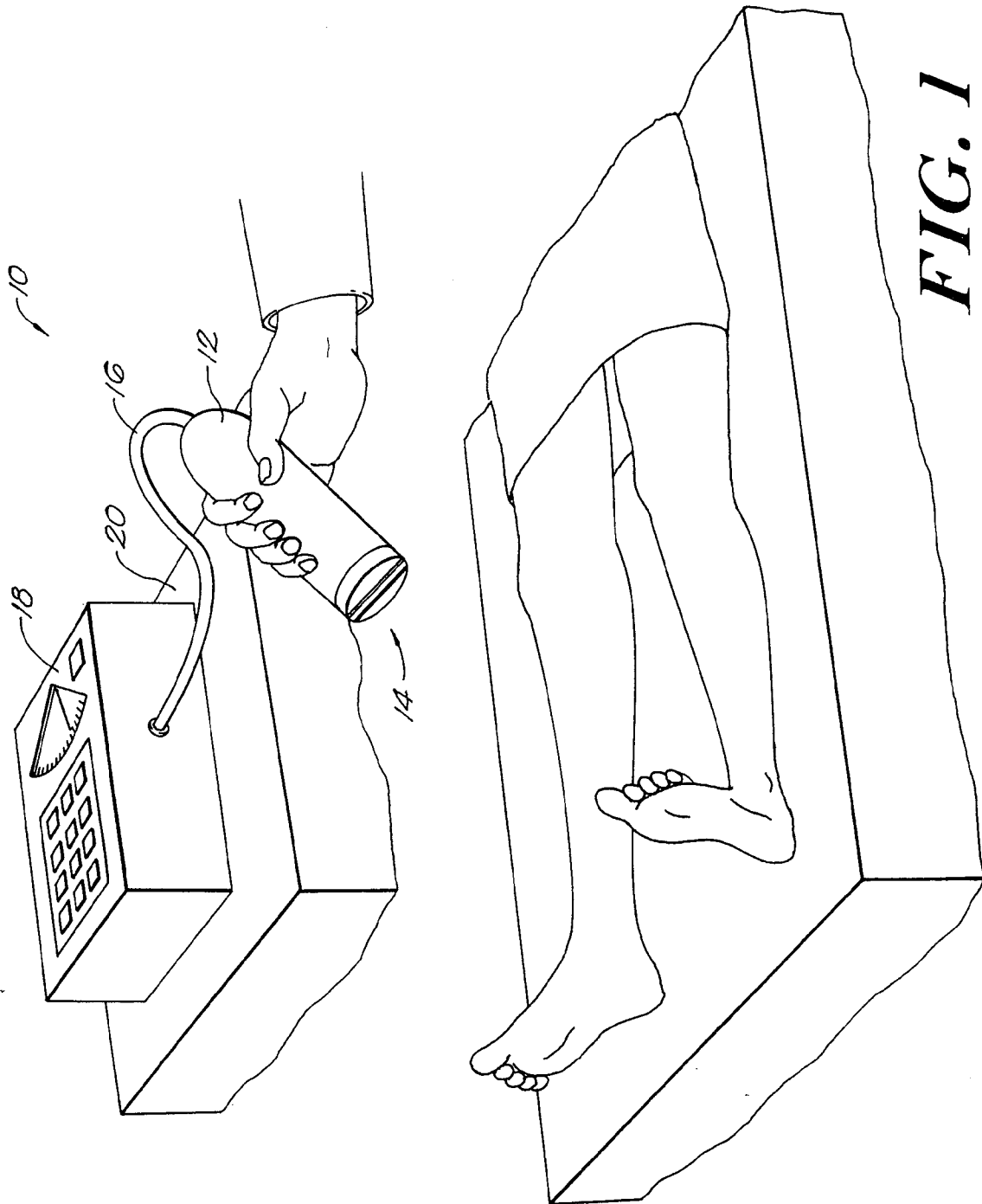
74. The kit of claim 73 wherein the kit further comprises a skin penetration enhancing apparatus.

10

75. The kit of claim 71 wherein the kit further comprises a particle removal apparatus.

76. The kit of claim 71 wherein the kit further comprises a protective shield for electrically conductive implants.

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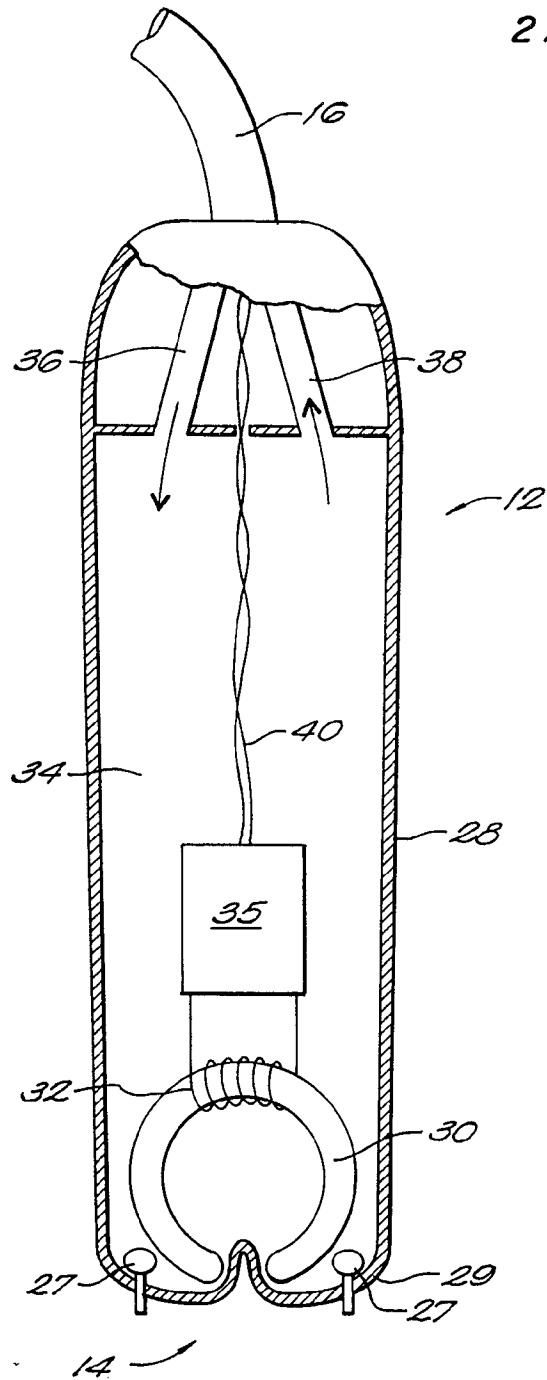


FIG. 2

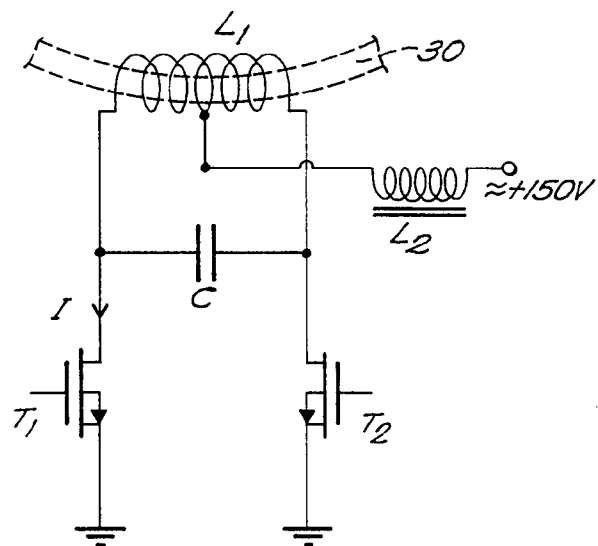
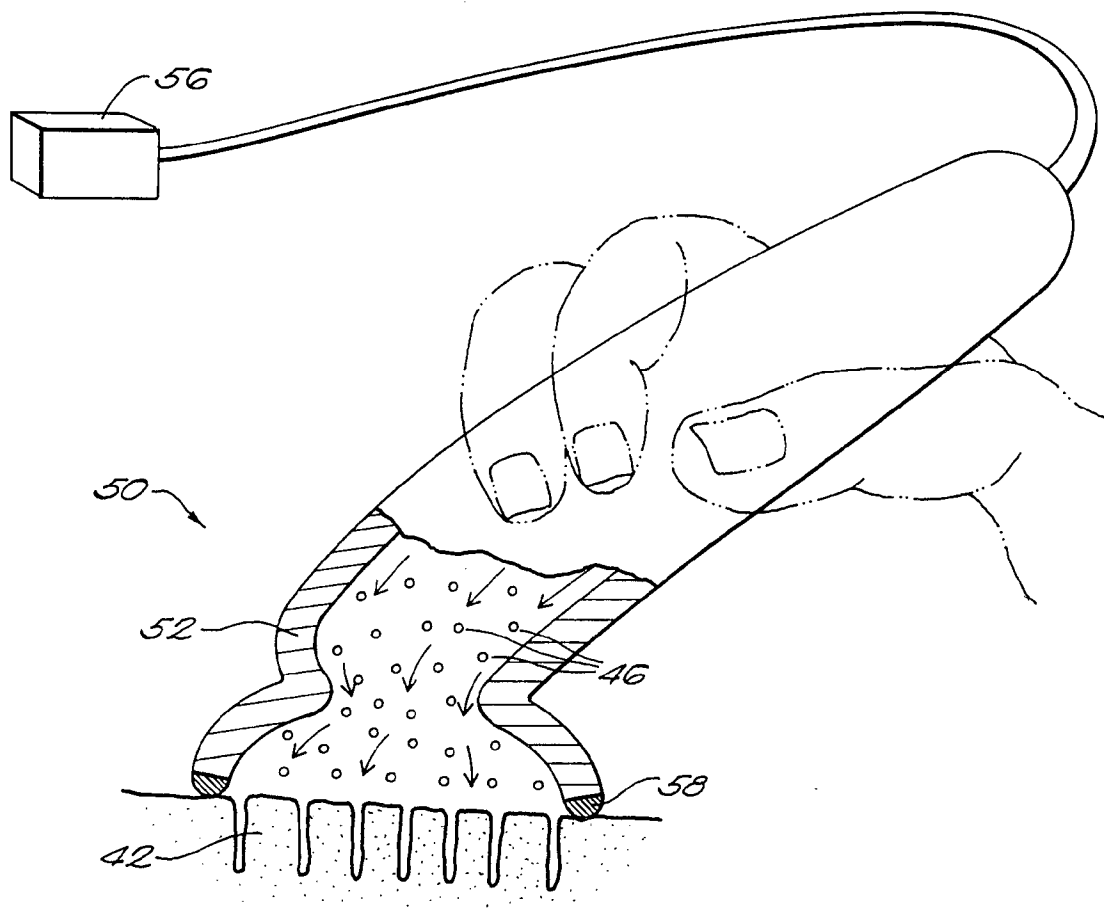
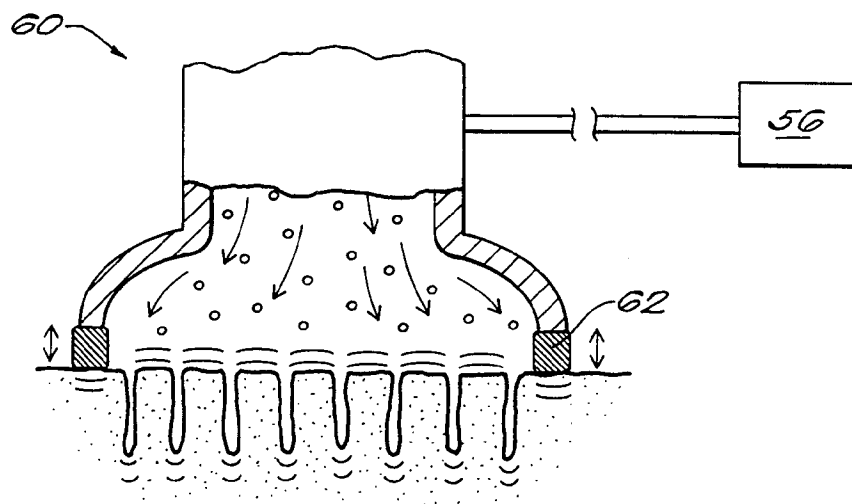
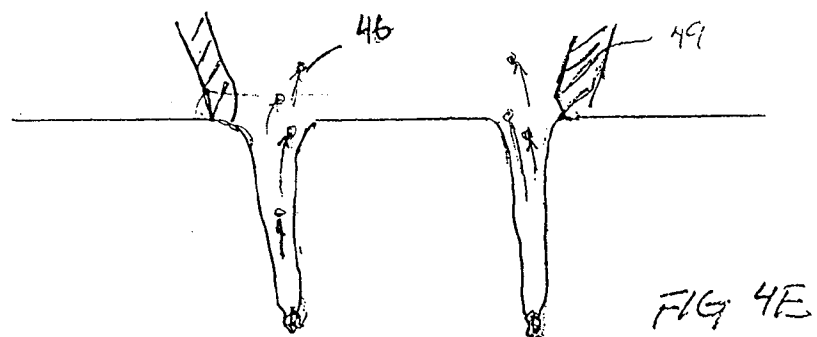
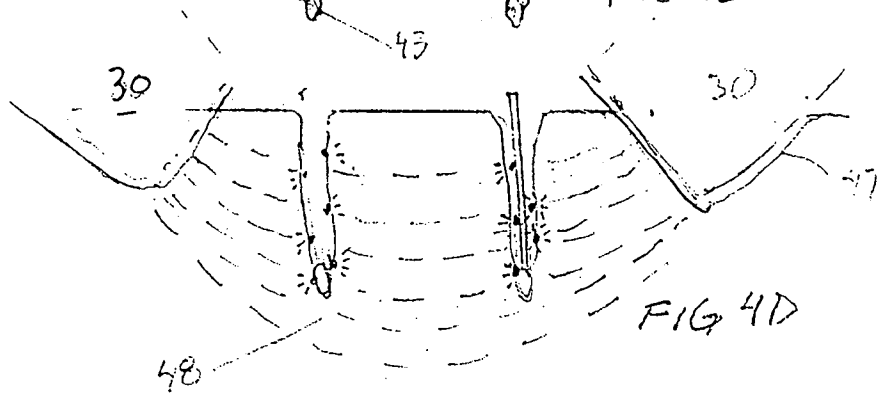
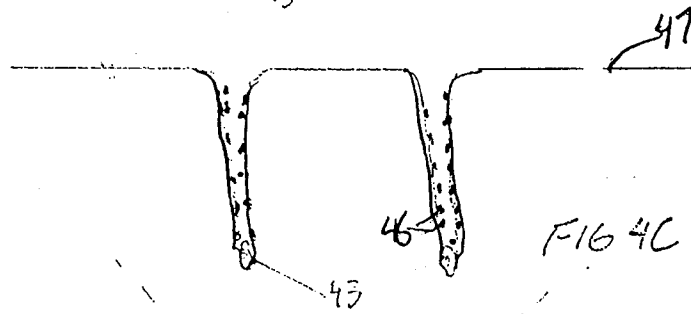
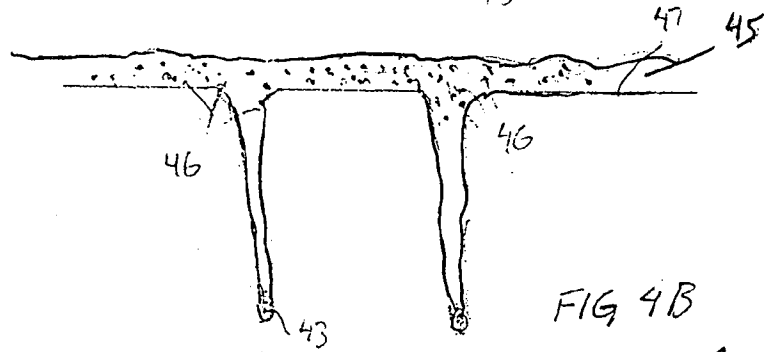
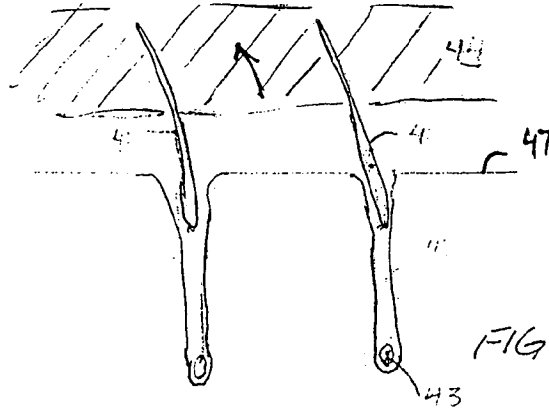
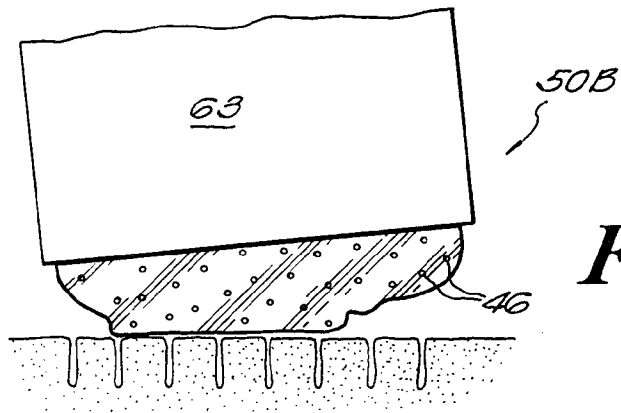
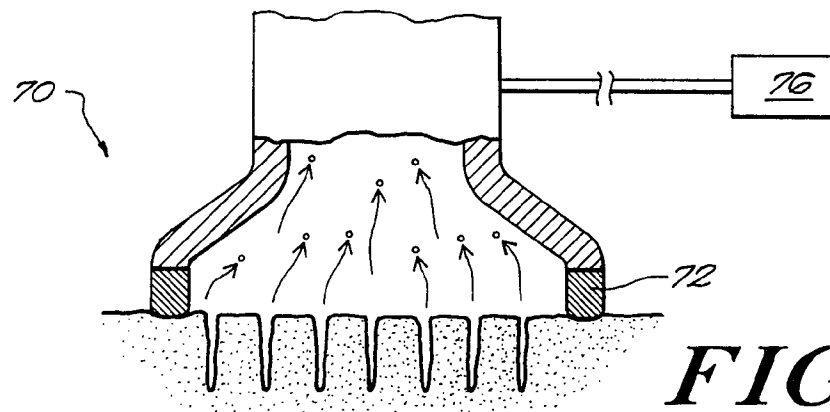
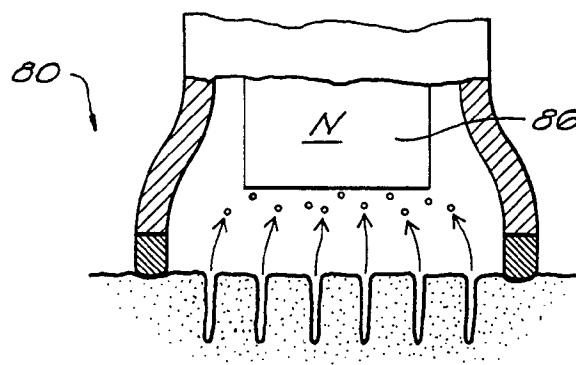


FIG. 3

**FIG. 5****FIG. 6**



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**FIG. 7****FIG. 8****FIG. 9**

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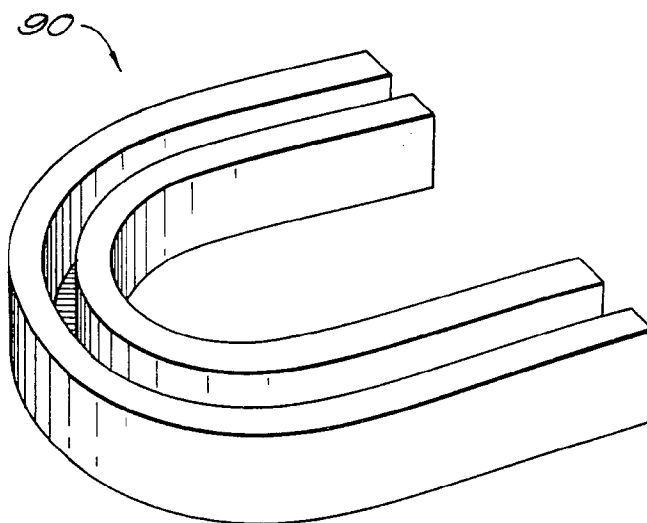


FIG. 10



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(21) International Application Number: PCT/US99/04929 (22) International Filing Date: 5 March 1999 (05.03.99) (30) Priority Data: 60/077,135 6 March 1998 (06.03.98) US (71) Applicants (for all designated States except US): SPECTRX, INC. [US/US]; 6000A Unity Drive, Norcross, GA 30071 (US). ALTEA TECHNOLOGIES, INC. [US/US]; 6015A Unity Drive, Norcross, GA 30071 (US). (72) Inventor; and (75) Inventor/Applicant (for US only): EPPSTEIN, Jonathan, A. [US/US]; 2844 Jasmine Court, Atlanta, GA 30345 (US). (74) Agents: FLOAM, D., Andrew et al.; Needle & Rosenberg, P.C., 127 Peachtree Street, N.E., Atlanta, GA 30303 (US).		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>	
(54) Title: PHOTOTHERMAL STRUCTURE FOR BIOMEDICAL APPLICATIONS, AND METHOD THEREFOR			
(57) Abstract			
<p>A photothermal structure designed for the uniform application of a photothermal material, such as, for example, a dye or a pigment, to a tissue, e.g., the stratum corneum. In one embodiment, the photothermal structure comprises photothermal material combined with a carrier, such as, for example, an adhesive or an ink, and the resulting combination is applied to a substrate, such as, for example, an inert polymeric substrate to form a photothermal structure. In another embodiment, the photothermal structure comprises photothermal material incorporated into a film-forming polymeric material.</p>			

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**PHOTOTHERMAL STRUCTURE FOR BIOMEDICAL
APPLICATIONS, AND METHOD THEREFOR**

This application claims the priority benefit of U.S. Provisional Application No.
5 60/077,135 filed March 6, 1998.

BACKGROUND OF THE INVENTION

Field of the Invention

This invention relates to a photothermal structure that is useful for the thermal
ablation of tissue, such as for the creation of micropores.

10 **Discussion of the Art**

Traditional glucose monitoring devices operate on the principle of taking blood
from an individual by a variety of methods, such as by needle or lancet. An individual
applies a drop a blood to a strip which contains chemistry that interacts with the blood.
The strip is inserted into a blood-glucose meter for measurement of glucose
15 concentration based on a change in reflectance of the strip.

There are alternative glucose monitoring technologies being developed to
provide a less invasive monitoring technique. One such technology involves measuring
the level of glucose in interstitial fluid. In order to obtain samples of interstitial fluid,
the barrier function of the stratum corneum must be overcome.

20 U.S. Patent Application Serial No. 08/776,863 entitled "Microporation Of
Human Skin For Drug Delivery and Monitoring Applications," filed February 7, 1997,
to Eppstein et al., discloses a method of ablating the stratum corneum to form at least
one micropore by treating a selected area of the stratum corneum with an effective
amount of an optical absorbing compound that exhibits strong absorption over the
25 emission range of a light source and thermally ablating the stratum corneum by
optically heating the optical absorbing compound. Heat is conductively transferred by
the compound to the stratum corneum to elevate the temperature of tissue-bound water
and other vaporizable substances in the selected area above the vaporization point of
water and other vaporizable substances. This technique is hereinafter referred to as
30 optical thermal ablation. Another microporation technique disclosed in that application
involves the use of a solid thermal probe that is applied directly to the tissue. To the

subject, these techniques are much less painful than using a lancet, if not completely painless.

In order to optimize the performance of the optical thermal ablation technique, it is desirable to accurately dispose a quantity of optical absorbing compound in contact
5 with the tissue to be treated.

SUMMARY OF THE INVENTION

Briefly, the present invention is directed to a method and structure for the uniform application of a photothermal or photothermal material, such as, for example, a dye or a pigment, to a tissue, e.g., the stratum corneum, for the purpose of photothermal
10 treatment of the tissue. In one embodiment, the photothermal structure comprises a photothermal material that is combined with a carrier, such as, for example, an adhesive or an ink, and the resulting combination is applied to a substrate, such as, for example, an inert polymeric substrate to form a photothermal structure. Means of application of the photothermal material to the carrier include, but are not limited to, printing,
15 spraying, and casting. In another embodiment of a photothermal structure, the photothermal material may be incorporated into a film-forming polymeric material, and the resulting mixture can then be processed to form a film. The photothermal structure of either embodiment is placed in contact with the tissue, e. g., the stratum corneum, and illuminated with a light source, such as a laser.

20 The above and other objects and advantages of the present invention will become more readily apparent when reference is to made to the following description, taken in conjunction with the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is an enlarged longitudinal cross-sectional view of a device supporting a
25 photothermal structure according to the present invention.

FIGs. 2 and 3 illustrate the use of the photothermal structure according to the present invention.

DETAILED DESCRIPTION OF THE DRAWINGS**Definitions**

As used herein, the expression "biological fluid" is intended to include blood serum or whole blood as well as interstitial fluid. "Interstitial fluid" is the clear fluid that occupies the space between the cells in the body. The term "stratum corneum" means the outermost layer of the skin, consisting of from about 15 to about 20 layers of cells in various stages of drying out. The stratum corneum provides a barrier to the loss of water from inside the body to the external environment and from attack from the external environment to the interior of the body. The term "epidermis" means the metabolically active region of the skin. It is found just below the stratum corneum and is approximately 10 times as thick as the stratum corneum. The epidermis does not contain blood. The term "dermis" means the region of skin approximately 10 times as thick as the epidermis and found just below the epidermis. The dermis contains large amounts of collagen, which provides structural integrity to the skin. The dermis contains a layer of small blood capillaries that provide oxygen and nutrients to the rest of the layers of skin.

As used herein, the term "tissue" means an aggregate of cells of a particular kind, together with their intercellular substance, that form a structural material. At least one surface of the tissue must be accessible to electromagnetic radiation so that one embodiment of the invention can be carried out. The preferred tissue is the skin. Other tissues suitable for use with this invention include mucosal tissue and soft organs.

As used herein, "ablation" refers to the process of controlled removing a selected area of tissue from the surrounding tissue by kinetic energy released when vaporizable substances in the selected area is elevated above the vaporization point of water and other vaporizable substances thereby removing some of the tissue in the selected area.

As used herein, "poration," "microporation," or any such similar term means the formation of a small hole or pore to a desired depth in or through a biological membrane, such as skin or mucous membrane, or the outer layer of an organism to lessen the barrier properties of this biological membrane to the passage of biological

fluids, such as analytes from within the biological membrane or the passage of permeants or drugs from without the biological membrane into the body for selected purposes, or for certain medical or surgical procedures

As used herein, the expressions "photothermal material" means a compound or
5 mixture of compounds that absorb electromagnetic radiation and radiate thermal energy and are capable of transferring thermal energy by conduction.

As used herein, the expressions "photothermal structure" or "photothermal assembly" means a structure comprising at least one layer containing a photothermal material. The structure may take the form of a film, sheet, block, membrane, gel,
10 woven fabric, non-woven fabric, or combination of the foregoing. As used herein, the term "polymer" means a compound containing repeating structural units. The repeating structural units, i. e., monomers, include, but are not limited to, cellulose, alkylene, ester, carbonate, amide, acrylic, agar, vinyl, and the like. As used herein, the term "adhesive" means a compound, or mixture of compounds, that promote adhesion
15 between two surfaces.

As used herein, the term "integrated device" means a device suitable for microporating (when coupled to a suitable energy source) tissue, collecting a biological fluid from the tissue (preferably through the micropores so created) and analyzing the biological fluid to determine a characteristic thereof.

20 The term "heated probe" means a probe, preferably solid phase, which is capable of being heated in response to the application of electrical or electromagnetic (optical) energy thereto. For simplicity, the probe is referred to as a "heated probe" which includes a probe in a heated or unheated state, but which is heatable.

The microporation technique described herein is further described in co-pending
25 U.S. Application Serial No. 08/776,863, filed February 7, 1997, entitled "Microporation of Human Skin for Drug Delivery and Monitoring Applications," the entirety of which is incorporated herein by reference.

FIG. 1 illustrates an integrated tissue poration, fluid harvesting and analysis device, shown at reference numeral 10, that supports a photothermal structure according
30 to the present invention. The device 10 comprises a tissue-contacting layer 12, which is

designed to be placed in contact with tissue, such as skin, mucosal tissue, etc. The photothermal structure occupies a portion of the tissue-contacting layer 12, and is shown at reference numeral 22. An optional fluid-transporting layer 18 may be provided to transport biological fluid, such as interstitial fluid, by means of chemically aided wicking. A meter-interface layer 20 overlies the fluid-transporting layer 18 and supports a sensor 28 to contact the collected biological fluid for analysis.

Electromagnetic (e.g., optical) energy is projected through the meter-interface layer 20 onto the photothermal structure 22 on the tissue-contacting layer 12. Accordingly, the meter-interface layer 20 either has an opening 24 formed therethrough, or an entirety or sufficient portion of the meter-interface layer 20 is made of material transparent to electromagnetic energy at wavelengths used to heat the photothermal structure 22.

Further details about the device 10 are disclosed in U.S. Provisional Application No. 60/007,135, the entirety of which is incorporated herein by reference.

The photothermal structure 22 is capable of absorbing electromagnetic energy from a source, such as a laser or other optical source, to heat up and transfer the heat to the stratum corneum, forming a micropore in the skin, at a controlled and desired depth.

The photothermal structure 22 comprises a photothermal material provided in such a manner that it can be applied to tissue in a reproducible manner. This ensures that the quantity of photothermal material to which the tissue is exposed can be known accurately.

Photothermal materials suitable for use in this invention are capable of absorbing electromagnetic radiation at one or more wavelengths. Electromagnetic radiation considered to be suitable for this invention include radiation from the ultraviolet, visible and infrared regions of the electromagnetic spectrum. It is preferred, however, that visible radiation and infrared radiation be employed. Ultraviolet radiation has a wavelength ranging from about 10 nm to about 380 nm. Visible radiation has a wavelength ranging from about 380 nm to about 780 nm. Infrared radiation has a wavelength ranging from about 780 nm to about 50,000 nm.

Photothermal materials suitable for use in this invention include, but are not limited to,

dyes and pigments. The term "pigment" is used to describe the class of colorants that are practically insoluble in the media in which they are applied. Pigments retain a particulate form, suspended in the media. The term "dye" is used to describe colorants that are soluble, or at least partially soluble, in the media in which they are applied.

- 5 Dyes exhibit an affinity to the substrate to which they are applied. Classes of dyes that are suitable for use in this invention include, but are not limited to, diphenylmethane dyes, methin-polymethine dyes, porphine dyes, indathrene dyes, quinones, dithiol metal complexes, dioxazines, dithiazines, polymeric chromophores. Classes of pigments that are suitable for use in this invention include, but are not limited to, carbon black,
10 carbon based pigments, metals, metal sols, dyed latexes, and inorganic pigments. Colorants that are preferred for this invention include copper phthalocyanine, indocyanine green, nigrosin, prussian blue, colloidal silver (20 to 100 nm diameter), carbon black, IR-780, IR-140, irgalan black, naphthol green B, tellurapyryllium, and vanadyl tetra-t-butyl-naphthalocyanine. In either case, particles of the dyes or pigments
15 must be of a size that they can readily be blended with carrier materials. It is preferred that the particles of dyes and pigments have a major dimension, e. g., length, diameter, no greater than about 50 μm and preferably less than 5 μm .

The photothermal material preferably does not melt or decompose at temperatures below about 120° C, and is capable of absorbing an amount of
20 electromagnetic energy and converting it to an amount of thermal energy sufficient to cause ablation of the tissue by the mechanism of conduction.

In one embodiment of this invention, the photothermal material is applied to the tissue-contacting layer 12 by means of a carrier. The tissue-contacting layer 12 serves as a substrate. The carrier is a material in which the photothermal material can be
25 uniformly dissolved if the photothermal material is a dye, or uniformly suspended if the photothermal material is a pigment. Carrier materials suitable for use with dyes and pigments include, but are not limited to, solid polymers, adhesives, gels, liquids, glass, oils, greases and paper. These materials may comprise polymeric materials such as acrylics, silicones, polyesters, polycarbonates, polyimides, cellulose, polyvinyl
30 derivatives, polyethylene, polypropylene, and the like.

The concentration of photothermal material in the carrier can vary. A sufficient concentration of dye is typically that required to obtain an optical density greater than 1.0 at the wavelength of the laser. Determination of the appropriate concentration can readily be determined by trial-and-error by one of ordinary skill in the art.

5 In addition to the photothermal material, other ingredients that can be added to the carrier, but are not limited to, plasticizers, surfactants, binders, and crosslinking agents. These materials are commercially available.

In general, substrates to which the carrier containing the photothermal material can be applied (i.e., the tissue-contacting layer) include, but are not limited to,
10 polymeric materials, cloth, non-woven materials, microporous membranes, glass, and metal foils. The substrate is preferably sufficiently flexible to allow close contact with the tissue. The substrate should adhere sufficiently to the carrier so that it does not detach before or during use. Materials that are suitable for preparing the substrate include, but are not limited to, polyesters, polyimides, polyethylenes, polypropylenes,
15 polycarbonates, acrylics, cellulose, derivatives of cellulose, and the like.

In another embodiment, the photothermal material is blended with a film-forming material which forms the tissue-contacting layer 12. The film-forming material is preferably capable of being formed into a film that will allow uniform suspension of the photothermal material and will allow sufficient flexibility to conform
20 to the tissue of the subject. Film-forming materials suitable for use in this embodiment include, but are not limited to, polyesters, polyimides, polyethylenes, polypropylenes, polycarbonates, acrylics, cellulose, derivatives of cellulose, and the like. Other substances can be combined into the suspension with the photothermal material, such as flux enhancer compounds that can be vaporized when the photothermal structure is
25 heated, thereby being released into microporated tissue for acting on the tissue.

The thickness of the tissue-contacting layer 12 is not critical, but preferably ranges from about 0.05 mm to about 2.0 mm. The surface dimensions of this layer are not critical, but the major dimension preferably ranges from about 5 mm to about 60 mm and the minor dimension preferably ranges from about 5 mm to about 60 mm. The
30 tissue-contacting layer 12 is shown as being rectangular, but other shapes are also

suitable, e. g., circular, elliptical, triangular, square, and other shapes, and the same is true for the photothermal structure 22. The tissue-contacting layer 12 can be adhered to the skin of the subject by means of adhesive, electrostatic force, or pressure applied by the subject. The seal between the skin and the tissue-contacting layer 12 is preferably
5 sufficiently tight so that biological fluid does not leak through or into it.

There are several ways to prepare the tissue-contacting layer 12 with the photothermal structure 22. According to one method, a pigment, e.g., carbon black, can be suspended uniformly into a pressure-sensitive adhesive composition. The adhesive composition can then be cast, or printed, onto a polymeric substrate. The adhesive
10 composition can then be cured. According to another method, a dye, e. g., copper phthalocyanine, can be suspended in an organic solvent, e.g., ethanol. The suspension can be applied to one side of a polymeric membrane by means of an air-brush. The film can then be allowed to dry. According to still another method, a pigment, e.g., carbon black, can be suspended in a polymer based ink, such as clear nail polish. The
15 ink can then be cast, or printed, onto a polymeric substrate. The film can then be cured. According to yet another method, a pigment, e.g., carbon black, can be blended into a polymeric material, e.g., linear low density polyethylene. The blend can then be melted and extruded into a film. The film can then be cured.

The photothermal structure has utility in many applications, including, but not
20 limited to, the integrated device disclosed herein. The photothermal structure can be applied to the tissue in a variety of ways. In the case of the photothermal structure mixed with a carrier, the carrier can be a pressure-sensitive adhesive, which adheres the assembly to the tissue. In the case of the film, the film can be adhered to the tissue by means of electrostatic force. Other means of attachment include pressure applied to the
25 film and vacuum to evacuate the area between the film or photothermal structure and the tissue to draw the film into contact with the tissue. Combinations of means of attachment can also be used.

The photothermal structure of the present invention overcomes several problems of the prior art, in particular in the manner of application. Specifically, pastes, or
30 suspensions, of photothermal material have been applied topically to the target tissue.

These materials have led to non-uniform and uncontrolled exposure to radiation from the laser. Variable and inaccurate application of the photothermal material can lead to unreproducible results of the photothermal treatment.

In addition, previous methods of applying a photosensitive dye to tissue give
5 rise to difficulty in removing the excess dye following photothermal treatment. This difficulty also brings about the potential for contamination of adjacent tissue, clothing, etc., with residual dye.

The photothermal structure according to the present invention deploys
photothermal material in such a manner that it can be readily removed from the tissue
10 and discarded following photothermal treatment. Moreover, the photothermal structure deploys a photothermal material with reproducible results.

The following are examples of the photothermal structure.

Example 1

Carbon black (20 nm) was suspended uniformly into an acrylic-based, pressure-
15 sensitive adhesive (Aroset A 1081, Ashland Chemical) to provide a suspension having a concentration of 20 g carbon black/liter. The resulting suspension was cast onto a polyester film (25 μ m thick). The adhesive was then cured by heating. After curing, the adhesive layer was approximately 50 μ m thick. The combination of carbon black-
adhesive and film substrate constituted the photothermal structure. A 0.4 inch diameter
20 circle of the photothermal structure was prepared and placed on the volar forearm of the subject. Light from a 1 Watt, CW laser diode of 810 nm (Coherent Inc., Santa Clara CA, part #S-81-100C-100T) was collimated and focused to a spot size of approximately 80 μ m in diameter at the plane of the surface of the skin. At 250 mW peak power at the skin, 30 pulses of 50 msec each were delivered, each with 80 msec delays between
25 pulses. The pulsing sequence was repeated to produce 6 photothermally treated sites spaced on the circumference of a 1.0 mm circle. After removal of the photothermal structure, the presence of the resulting small pores in the stratum corneum could be detected or observed.

Example 2

Carbon black ($< 1 \mu\text{m}$) was suspended into an acrylic-based ink, such as clear nail polish, to provide a suspension having a concentration of 10 g/l. The suspension was then cast, or printed, onto a polyester substrate (0.050 mm thick). The suspension was cured. The resulting coated substrate was then applied topically to the skin either directly, as a film, or, indirectly, as part of a device. Light from a laser or from a polychromatic light source was focused onto the film and interface between the colorant and the skin for the photothermal treatment. Following the photothermal treatment, the film was removed and discarded.

Example 3

Carbon black ($< 1 \mu\text{m}$) was blended into polyester to provide a blend having a final concentration of 10 g/l. The blend was commercially available under the trade designation "MELINEX 427/200." The blend was melted, and the melted blend was then extruded to form a film (0.050 mm thick). The film was then cured. The resulting film was then applied topically to the skin, either directly as a film or indirectly as part of a device. Light from a laser or from a polychromatic light source was focused onto the film and interface between the colorant and the skin for the photothermal treatment. Following the photothermal treatment, the film was removed and discarded.

Example 4

Titanium metal was sputter-coated onto a polycarbonate film substrate. The substrate has a thickness of 2 mil (0.05 mm). The thickness of the titanium/titanium oxide layer was approximately 50 nm. The film was placed onto the skin, the metal layer being in contact with the skin. The film was maintained in proper position by an adhesive ring, which surrounded the targeted area. Light from a laser or from a polychromatic light source was focused onto the film and interface between the colorant and the skin for the photothermal treatment. Following the photothermal treatment, the film was removed and discarded.

The metal layer can be coated with a thin layer of polymeric material, such as 0.25 mil (0.006 mm) of polyoxymethylmethacrylate, as a protective layer.

Example 5

The photothermal structure of Example 1 was placed onto the skin over the area to be treated. Light from a laser was focused onto the assembly to create a small region of thermally treated stratum corneum. The treated region was characterized by loss of
5 adhesion of underlying cells. The region appears as a small pore surrounded by an area of loose skin, or an area resembling a small blister in which the cell adhesion in the epidermal layer has been disrupted. This treatment was repeated such that the individually treated areas overlap. When the adhesive was removed, the treated stratum corneum and some of the epidermis underlying the stratum corneum was removed.
10 Remaining epidermis may be removed by mild abrasion with a sterile cotton swab. The treatment generally does not result in bleeding.

Example 6

The method described in Example 5 was performed with an adhesive-free photothermal structure. Following photothermal treatment, the affected tissue was
15 removed by mild rubbing with a cotton swab or by applying a sterile adhesive film, which can remove the tissue with the removal of the tape.

Example 7

A small vacuum chamber having an orifice of 9 mm in diameter was placed over the skin, covering the 6 micropores, formed according to the procedures of
20 Example 1. The chamber was evacuated to -6.00 psi for a period of two minutes. After the vacuum was released, the resulting clear fluid was collected by means of a micro-capillary tube. Volumes of 0.25 to 0.75 μ l were routinely obtained through use of this protocol. The presence of fluid indicated that the photothermally generated pores had penetrated the stratum corneum into the underlying epidermis, breaching the barrier
25 properties of the stratum corneum. No measurable fluid was obtained with application of the vacuum to untreated skin.

Example 8

Samples of interstitial fluid were obtained as described in Example 7. The clear fluid was diluted into 1.0 ml of 5 mM phosphate, 0.02% sodium azide, pH 7.0. At the
30 same time of sampling the interstitial fluid, blood plasma samples were obtained from

the same subject. The finger of the subject was pierced with a lancet device, and blood was collected into a capillary tube containing heparin. The blood sample was centrifuged to separate the plasma fraction from the cellular fraction. A sample of 1.0 μ l of plasma was transferred to 1.0 ml of phosphate buffer diluent by means of a micro capillary tube. The dilute samples of interstitial fluid and plasma were analyzed for glucose content by means of high pressure liquid chromatography with pulsed amperometric detection (HPLC-PAD). HPLC-PAD analysis was performed by using a Dionex PA-1 column, 4.0 x 250 mm, operated with a flow rate of 1.0 ml/min with 150 mM sodium hydroxide. Injection volumes of 10 μ l were made. Glucose demonstrated a peak retention time of 4.0 ± 0.3 minutes. Samples were compared to known aqueous and serum standards containing glucose, and concentrations were determined from the area of the glucose peak. The results contained from six healthy, non-diabetic subjects are set forth in the following table, where the units of glucose are mg/dl.

Subject	Glucose in interstitial fluid	Glucose in plasma
A	102	116
B	123	143
C	147	123
D	113	120
E	88	94
F	102	105

Example 9

To demonstrate the ability to deliver substances through the stratum corneum, sodium fluorescein was used as a model tracer. The volar forearm of a test subject was treated as in Example 1 to prepare a set of 6 pores comprising a circular pattern approximately 1.1 mm in diameter. Following poration, 1.0 μ l of 10% sodium fluorescein in sterile saline was placed on the skin, covering the pores. A control area of skin, free of formed pores, was similarly covered with 1.0 μ l of sodium fluorescein solution. After two minutes, the excess solution was removed by blotting, followed by washing with mild detergent, rinsing, and blotting dry. Where pores were formed, the skin demonstrated visible pigmentation due to the presence of fluorescein within the

tissue. The area of yellow staining was approximately 1.4 mm in diameter. No staining was apparent for the control area. Under ultraviolet illumination, the area of the skin where pores were formed demonstrated intense yellow-green fluorescence covering an area of approximately 1.5 mm in diameter, due to the presence of the sodium fluorescein. The immediate area which outlined each of the six pores was more intensely fluorescent. In addition, there was a light fluorescence covering an area of approximately 2.0 mm in diameter which appeared to be due to some residual fluorescence in the outer stratum corneum.

FIGs. 2 and 3 illustrate the operation and use of the photothermal structure. The photothermal structure can be used to form a micropore in the stratum corneum. Generation of small pores in the stratum corneum may be used to gain access to body fluids for diagnostic applications. Additionally, poration may be used to increase the permeability of some drugs or other bioactive agents. The photothermal structure according to the present invention may also be applied in surgical applications such as the treatment of surface lesions, tattoos, or other photothermal treatments of tissue surfaces.

In operation, the photothermal structure is placed against a surface of the tissue, such as skin, as shown in FIG. 2. A source of electromagnetic energy, such as optical energy, is activated and the energy is focused on the photothermal structure. After an appropriate period of time, e.g., from about 10 ms to about 1 second, the energy heats the photothermal structure 22, and the thermal energy in the photothermal structure 22 is transferred to the tissue to ablate the tissue and form at least one micropore 50 as shown in FIG. 3. In the example of FIG. 3, two micropores 50 are formed in the stratum corneum ("SC"), and the micropores may go as deep as through the epidermis ("E") and into the dermis ("D"). At the locations on the photothermal structure where the optical energy is focused, the photothermal structure melts or is burned so that small holes 60 are created. Biological fluid traverses the stratum corneum through the micropore 50 can be collected for analysis. For example, when the photothermal structure is employed in an integrated device such as that shown in FIG. 1, the

biological fluid is collected and analyzed by the same apparatus that forms the micropores.

Sources of electromagnetic energy that are suitable for use with the photothermal structure according to the present invention are disclosed in U.S. Patent
5 Application Serial No. 08/776,863.

In summary, the photothermal structure, in one embodiment, comprises a quantity of photothermal material; a carrier which is combined with the photothermal material such that the photothermal material is substantially uniformly dissolved or suspended therein; and a substrate to which the carrier-photothermal material
10 combination is applied. A layer of priming material may be provided between the substrate and the carrier. In another embodiment, the photothermal structure comprises a quantity of photothermal material; and a film material containing a substantially uniform suspension of the photothermal material.

Further, a method for treating tissue is provided, which comprises the steps of
15 applying a photothermal structure including a quantity of photothermal material to tissue, and subjecting the photothermal structure to electromagnetic radiation. The step of applying may comprise applying a substrate, to which is applied a carrier incorporating a substantially uniform suspension of the photothermal material. The substrate may be adhered to the tissue. Alternatively, the step of applying may involve
20 applying a film incorporating a substantially uniform suspension of the photothermal material.

Various modifications and alterations of this invention will become apparent to those skilled in the art without departing from the scope and spirit of this invention, and it should be understood that this invention is not to be unduly limited to the illustrative
25 embodiments set forth herein.

What is claimed is:

1. A photothermal structure for treating tissue, comprising:
 - (a) a quantity of photothermal material;
 - (b) a carrier which is combined with the photothermal material such that the photothermal material is substantially uniformly dissolved or suspended therein; and
 - (c) a substrate to which the carrier-photothermal material combination is applied.
2. The photothermal structure of claim 1, and further comprising a layer of priming material between the substrate and the carrier.
3. The photothermal structure of claim 1, wherein the photothermal material is a dye or a pigment.
4. The photothermal structure of claim 1, wherein the carrier is one of a solid polymer, adhesive, gel and ink.
5. A photothermal structure for treating tissue, comprising:
 - (a) a quantity of photothermal material; and
 - (b) a film material containing a substantially uniform suspension of the photothermal material.
6. The photothermal structure of claim 5, and wherein the film material is made of one of polyesters, polyimides, polyethylenes, polypropylenes, acrylics, cellulose and derivatives thereof.
7. The photothermal structure of claim 6, wherein the photothermal material is a dye or pigment.
8. A method for treating tissue comprising the steps of:
 - (a) applying a photothermal structure including a quantity of photothermal material to the tissue; and
 - (b) subjecting said photothermal structure to electromagnetic radiation.
9. The method of claim 8, wherein the step of applying comprises applying a substrate to which is applied a carrier in which the quantity of photothermal material is substantially uniformly dissolved or suspended.

10. The method of claim 9, wherein the step of applying comprises adhering the substrate to the tissue.

11. The method of claim 8, wherein the step of applying comprises applying a film incorporating a substantially uniform suspension of the photothermal material.

12. The method of claim 8, wherein the electromagnetic radiation is in a wavelength range from about 10 nm to about 50,000 nm.

13. The method of claim 8, wherein said step of subjecting comprises emitting electromagnetic radiation from a polychromatic light source.

14. The method of claim 8, wherein said step of subjecting comprises emitting electromagnetic radiation from a laser.

15. The method of claim 8, and further comprising the step of withdrawing body fluids from an opening created by thermal ablation of the tissue.

16. The method of claim 15, and further comprising the step of determining the concentration of at least one analyte in the body fluids.

17. The method of claim 16, wherein the step of determining comprises determining the concentration of glucose.

18. The method of claim 8, and further comprising the step of introducing a permeant into said opening.

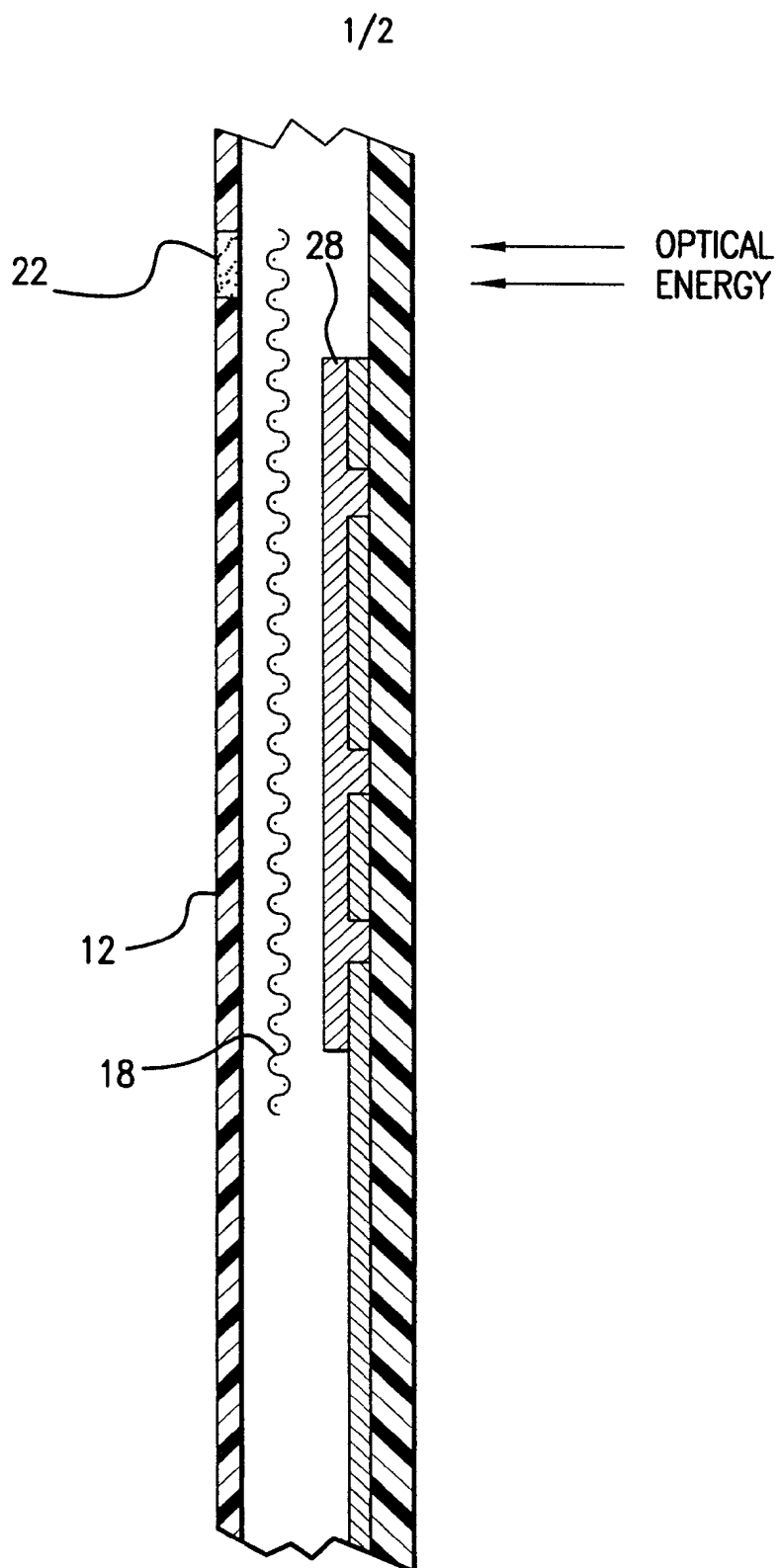


FIG.1

2/2

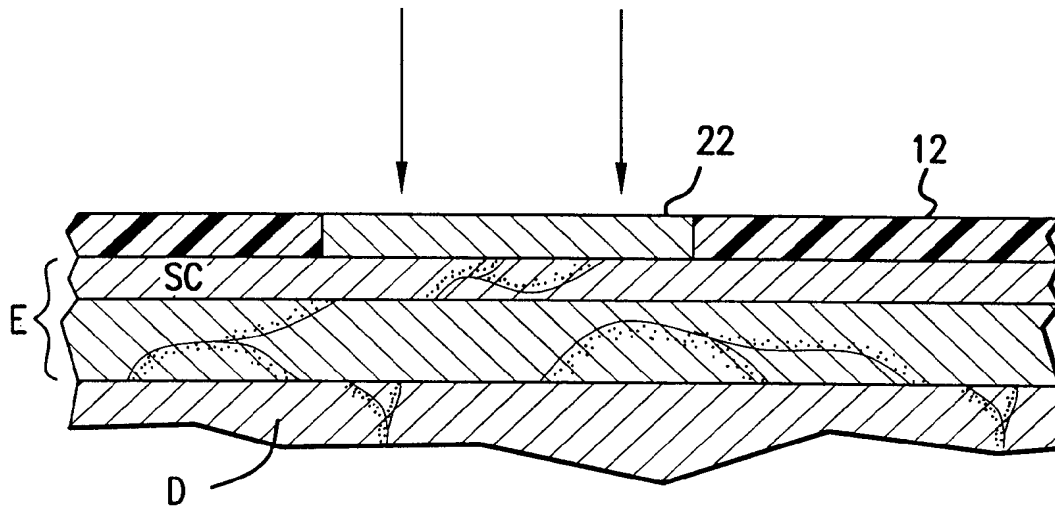


FIG.2

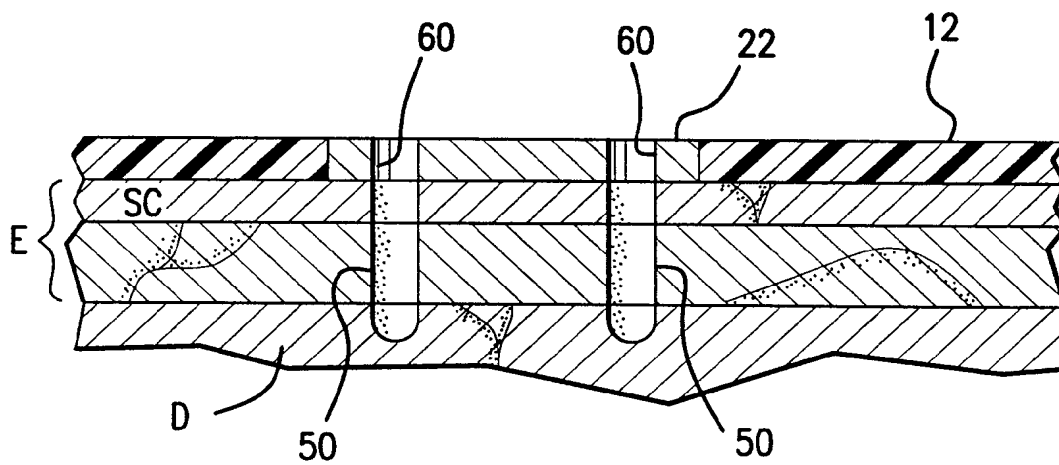


FIG.3

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/04929

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 A61K41/00 A61B10/00 A61M37/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61K A61B A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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X	<p>WO 97 07734 A (SPECTRX ET AL.) 6 March 1997 cited in the application see page 7, line 1 - page 9, line 13 see page 10, line 11 - line 19 see page 14, line 1 - page 16, line 28 see claim 6; examples 4,6,7 -----</p>	1-7
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☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

24 June 1999

Date of mailing of the international search report

06/07/1999

Name and mailing address of the ISA

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Authorized officer

Raybould, B

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/04929

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 8-18
because they relate to subject matter not required to be searched by this Authority, namely:
Rule 39.1 (iv) PCT - Method for treatment of the human or animal body by surgery
Rule 39.1 (iv) PCT - Method for treatment of the human or animal body by therapy
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

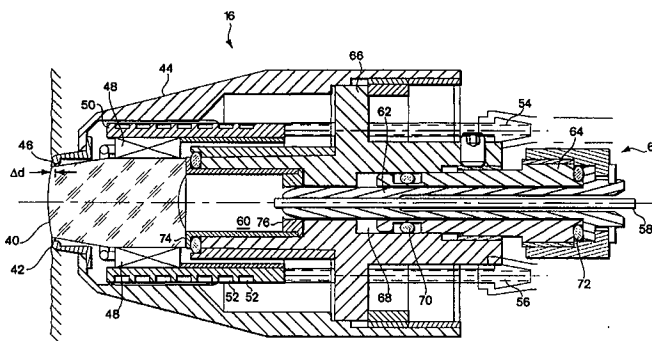
PCT/US 99/04929

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(54) Title: SYSTEM FOR ELECTROMAGNETIC RADIATION OF THE SKIN



(57) Abstract

A system for treating a selected dermatologic problem and a head for use with such system are provided. The head may include an optical waveguide having a first end to which EM radiation appropriate for treating the condition is applied. The waveguide also has a skin-contacting second end opposite the first end, a temperature sensor being located within a few millimeters, and preferably within 1 to 2 millimeters, of the second end of the waveguide. A temperature sensor may be similarly located in other skin contacting portions of the head. A mechanism is preferably also provided for removing heat from the waveguide and, for preferred embodiments, the second end of the head which is in contact with the skin has a reflection aperture which is substantially as great as the radiation back-scatter aperture from the patient's skin. Such aperture may be the aperture at the second end of the waveguide or a reflection plate or surface of appropriate size may surround the waveguide or other light path at its second end. The portion of the back-scattered radiation entering the waveguide is substantially internally reflected therein, with a reflector being provided, preferably at the first end of the waveguide, for returning back-scattered light to the patient's skin. The reflector may be angle dependent so as to more strongly reflect back-scattered light more perpendicular to the skin surface than back-scattered radiation more parallel to the skin surface. Controls are also provided responsive to the temperature sensing for determining temperature at a predetermined depth in the patient's skin, for example at the DE junction, and for utilizing this information to detect good thermal contact between the head and the patient's skin and to otherwise control treatment. The head may also have a mechanism for forming a reflecting chamber under the waveguide and drawing a fold of skin therein, or for providing a second enlarged waveguide to expand the optical aperture of the radiation.

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SYSTEM FOR ELECTROMAGNETIC RADIATION OF THE SKIN

Related Applications

5 This application is a continuation in part of application Serial No. 08/759,036, and of application Serial No. 08/759,136, both filed December 2, 1996, and of application Serial No. 09/078,055, filed May 13, 1998 and claims priority of provision application No. 60/077,794 and provisional application No. 60/115,447, filed January 8, 1999, which applications are all incorporated herein by reference.

Field of the Invention

10 This invention relates to the utilization of electromagnetic (EM) radiation for treating selected dermatologic problems, and more particularly to a system which utilizes temperature detection at a waveguide through which radiation is being applied to the patient's skin to perform
15 various control functions and to a head usable in such system or elsewhere, which head includes efficient reflectors for back-scattered radiation and/or for otherwise enhancing irradiation of a target volume containing the dermatologic problem.

Background of the Invention

20 Lasers, lamps and other sources of electromagnetic radiation are being increasingly utilized to treat various dermatological conditions, and in particular for the removal of unwanted hair, spider veins, leg veins, other veins or blood vessels which are visible through the patient's skin, lesions, port-wine stains, tattoos and the like. One problem with such treatments is that the only way to get the radiation to a target volume in the dermis where treatment is desired is to
25 transmit the radiation to such volume through the overlying epidermis. Further, since many of the treatments involve absorption of energy by melanin in the dermal volume being treated, for example in a hair follicle, and there is also melanin in the epidermis, particularly in the portion thereof at the dermal/epidermal (DE) junction, the EM radiation used for treatment is generally also absorbed to varying degrees in the epidermis. Further, the deeper in the dermis the treatment
30 is desired and/or the larger the element being treated, the more energy must be used, this generally involving use of a more powerful laser or other radiation source with higher fluence and/or operating such source for longer time durations. However, as the energy applied through

the epidermis increases, the potential for damage to the epidermis as a result of energy absorption therein also increases.

Therefore, one limitation on the energies which can be used for various dermatological treatments in the dermis, and in particular on the depths in the dermis at which treatment can be performed, and on the size of the elements which can be treated, is that the energy applied cannot be so high as to cause appreciable damage to the epidermis. Various ways around this problem have been proposed in the prior art, most of which involve some cooling of the epidermis prior to and/or during treatment to limit or prevent thermal damage thereto. Examples of such procedures include applying cryogenic or other cooling sprays to the skin, applying a cooling gel to the skin, applying radiation through a cold-pack in contact with the skin or through an applicator which is cooled by flowing water, flowing air, or the like. However, these prior art systems have not been wholly satisfactory. One reason for this is that, since most of the absorption is in the melanin located in the lower portions of the epidermis, it is desirable to have cooling through the entire epidermal layer, which is typically about 0.1 mm thick. However, it is not desirable that the cooling extend significantly below the DE junction into the dermal layer since cooling in the dermal layer can potentially inhibit the desired thermal damage to follicles, blood vessels or the like in this region. Further, there are significant variations in radiation absorption by a patients skin, not only among different individuals, people having darker skin absorbing more radiation and being more prone to epidermal damage than people with lighter skin, but even for different areas on the body of a single individual. Therefore, cooling which is not customized to the treatment area generally results in the cooling not being to the proper depth, a problem which can interfere with treatment and/or permit thermal damage to the epidermis.

It would therefore be desirable if the temperature at a selected depth in the skin, for example the DE junction, could be measured, and this temperature utilized to control skin temperature. for example through the epidermis, by some combination of controlling the laser energy applied to skin and/or controlling cooling applied to the skin. However, while infrared sensors have for example been utilized in the past to detect temperature at the surface of the skin, such detection does not provide an accurate indication of temperature even at the skin surface, these readings varying with such factors as skin layer thickness, skin roughness and skin color in addition to temperature. Infrared sensors also provide virtually no information as to skin temperature at a depth below the surface. Therefore, such detection has heretofore been used

only for gross controls, for example to turn off the laser if an emergency temperature threshold is exceeded or the like, but not to fine tune energy application and/or cooling so as to maintain a desired temperature at a selected depth, for example at the DE junction, thereby facilitating a desired treatment without epidermal damage.

5 A need therefore exists for an improved technique which permits more accurate determinations of skin temperature at various depths, including at the DE junction, so as to permit more accurate and more automatic control of EM radiation treatments for various dermatological conditions. In particular, because of variations in skin pigmentation, differences in epidermal depth, and other dermatological differences among patients, laser dermatology procedures are
10 now performed almost exclusively by physicians or other highly trained individuals, and such individuals must exercise great care to assure that epidermal damage does not occur, while still achieving the desired therapeutic effect. More accurate measurement of temperature at desired depths would make treatments by such skilled personnel easier to perform and would permit such procedures to be safely performed by less highly trained, and therefore less expensive, personnel.
15 Such skin temperature measurements could also be utilized to determine skin type/pigmentation for the patient and/or for the part of a patient's body being treated and/or for other purposes.

Where cooling of the epidermis is achieved by placing a cooled applicator or other cooled body in contact with the patient's skin, the contact must be made with sufficient pressure to assure good thermal contact between the cooled body and the skin. However, differences in skin
20 thickness and elasticity, differences in bone backing and other factors affect the pressure required to achieve good thermal contact for different patients and for different areas on the body for the same patient. This is another reason why highly trained and skilled individuals are required for performing the treatments and contributes to the high cost of the treatment. It would therefore be preferable if an automatic technique could be provided for detecting, and thus assuring, good
25 thermal contact between a cooling element and the patient's skin. Such a technique or mechanism, by assuring good thermal contact with the skin before the radiation source is fired, could solve two critical safety problems for radiation dermatology. First, it assures adequate cooling of the epidermis before heating thereof through energy absorption; and second, it assures that the radiation will not be accidentally applied to the eyes or other unwanted place.

30 Related but opposite problems arise in performing certain skin resurfacing/wrinkle removal procedures where the objective is to heat and destroy only the most surface layer of the skin, for example the epidermis, with minimal damage to underlying layers. This requires tight

control of factors such as laser energy, pulse duration and repetition rate. However, variations in patient's skin make such tight control difficult even for highly trained and skilled personnel. Similar problems also arise in other dermatological procedures involving lasers or other radiation sources.

5 Another related problem in using an EM radiation source for dermatological treatment is that the skin reflects back a significant portion of the radiation applied thereto. Since this reflected energy does not reach the treatment site, a higher energy radiation source is required to achieve the desired dermatological treatment than would be the case if a larger percentage of the applied radiation reached the treatment site. It has previously been suggested that one solution
10 to this problem is to provide a retro-reflector which collects and returns such back-scattered radiation to the patient's skin. However, existing retro-reflector devices have not optimized the collection and return of such back-scattered radiation and improved techniques for the more efficient reutilization of back-scattered radiation is therefore desirable. One particular problem with prior art retroreflectors is that they reflect all back-scattered radiation at substantially the
15 same angle the radiation was received; however, radiation at an angle more parallel than perpendicular to the skin surface generally does not reach the treatment area and therefore only heats the surface of the skin, contributing to thermal damage of the skin, without having any beneficial/therapeutic effect. A retroreflection technique which does not contribute to or increase this "parallel" radiation would therefore be desirable.

20 Two other factors can contribute to the efficiency of dermatologic treatments. The first factor is "spot size" or in other words the optical aperture of the applied radiation. Spot size is typically limited by the optics of the handpiece utilized and by the desired fluence as a function of the available energy source. However, a larger spot size permits treatment of large body areas such as back or legs to be accomplished much more quickly, something which enhances both
25 patient satisfaction and practitioner profitability. A technique for facilitating larger spot sizes is thus desirable.

Secondly, anything which reduces the distance from the irradiation source to the target area reduces the amount of energy required to achieve a desired therapeutic effect and anything which permits more of the applied energy to reach the target area has a similar effect. Techniques
30 which facilitate the achievements of these objectives are therefore also desirable.

Summary of the Invention

In accordance with the above, this invention provides both a system for treating a selected dermatologic problem and a head for use in such system. The head, for preferred embodiments includes an optical waveguide or other light path for directing EM radiation of a wavelength appropriate for treating the selected patient dermatologic problem to a first end of the waveguide, the waveguide also having a skin-contacting second end which is opposite the first end; and a sensor at the second end of the waveguide, or otherwise closely adjacent a skin-contacting surface of the head, which senses the temperature thereat. For preferred embodiments, the head also includes a mechanism for removing heat from the waveguide. In order to achieve commercially useful sensitivity, it is preferable that the sensor be located no more than a few millimeters from the skin-contacting surface of the head, for example, the second end of the waveguide, the end contacting the patient's skin. Therefore, for preferred embodiments, the sensor is located within 5 mm of the second end of the waveguide, and for the most preferred embodiments the sensor is located within 1 mm of the second end.

Where a mechanism for removing heat is provided, such mechanism preferably includes a thermoelectric device having one side in thermal contact with the waveguide and an opposite side in thermal contact with a temperature sink. For a preferred embodiment of the invention, back-scattered radiation is substantially internally reflected within the optical waveguide, and there is a reflector within the waveguide for returning back-scattered radiation through the waveguide to the patient's skin. While the reflector may be at a variety of locations within the waveguide, for a preferred embodiment, it is located at the first end of the waveguide. The reflector may also be along sides of the waveguide and the coefficient of reflection for areas of the reflector, either at the first end, the side walls or both, may be selected such that back scattered radiation which, before entering the waveguide, at angles nearer perpendicular to the patient's skin are reflected more strongly than backscattered radiation which, before entering the waveguide, are at angles more nearly parallel to the skin surface. The second end of the waveguide in contact with the patient's skin may also have an aperture which is at least substantially as great as the aperture of radiation back-scattered from the patient's skin or a "reflection aperture" substantially as great as the radiation back-scatter aperture may be achieved in other ways. For example, a reflector plate of size to provide the desired reflection aperture may surround the second end of the waveguide. More generally, the invention may include at least one waveguide passing through the head and terminating at a skin-contacting surface

thereof, EM radiation being applied through the at least waveguide path to the patient's skin; and a reflection means for returning back-scattered radiation to the patient's skin, which reflection means has a reflection aperture at least substantially as great as the radiation back-scatter aperture. Reflection means may include at least a portion of the skin-contacting surface of the head, which portion may be in the form of a reflection plate, and may also include at least one reflection surface for back-scattered radiation entering the waveguide, at least part of which surface may be in the waveguide.

The system may be for treating a selected dermatological problem in a selected volume of a patient's skin at a depth d which is below the DE junction. A source of EM radiation of a wavelength appropriate for treating the problem is provided along with an optical waveguide, a mechanism which cools the patient's skin, at least in the portion thereof in contact with the waveguide when the second end of the waveguide is in contact with the patient's skin, and a temperature sensor at the second end of the waveguide. The temperature at the sensor is indicative of the temperature at the patient's DE junction. Finally, controls are provided which are operative in response to the sensor indicating that the DE junction has been cooled to at least a selected temperature for permitting radiation from the source to be passed through the waveguide to the patient's skin. The cooling mechanism preferably removes heat from the waveguide; when in contact with the patient's skin, the waveguide removing heat from and thus cooling the skin. The controls may also be operative in response to the sensor for maintaining the DE junction within a selected temperature range during application of radiation to the patient's skin. The controls may also detect a selected temperature/time profile at the sensor, the profile being indicative of contact of the waveguide with the patient's skin, and may prevent radiation from passing to the patient's skin unless the predetermined profile is detected. This assures that radiation is not applied to the patient's skin unless there is good thermal contact between the radiation-applying waveguide of the head and the patient's skin. For preferred embodiments, the controls operate the cooling mechanism to cool the waveguide to a desired temperature, the controls being responsive to the sensor for determining when the desired temperature has been reached.

The controls may also be operative in response to the sensor sensing a selected increasing temperature profile at the sensor when the waveguide is placed in contact with the patient's skin for permitting radiation from the source to be passed through the waveguide to the patient's skin.

This control may be instead of the control based on detection that the DE junction has been cooled to a selected temperature, but is preferably in addition thereto.

The enhanced retro-reflector features discussed above may also be used in the head independent of the temperature measuring features previously discussed, but are preferably used in conjunction therewith. The invention may also include a head having at least one optical waveguide for receiving EM radiation and for directing it to a skin-contacting surface of the at least one waveguide and a standoff having a first and a second end, with the first end surrounding the at least one waveguide at its lower end and forming a substantially air-tight seal therewith. The second end of the standoff is adapted to be in contact with the patient's skin over the selected volume to form a chamber between the skin-contacting waveguide surface, the patient's skin and walls of the standoff. A means is also provided for creating negative pressure in the chamber to draw the patient's skin therein and into contact with the skin-contact surface. The walls of the standoff are preferable reflective to return back-scattered radiation to the patient's skin. The means for creating negative pressure may include a hose mounted at one end to open into the chamber and connected at its other end to a source of negative pressure. Alternatively, the means for creating negative pressure may include the walls of the standoff being deformable when pressure is applied to the head/waveguide to permit the skin-contacting surface of the waveguide to contact the patient's skin, forcing most of the air from the chamber, with the walls of the standoff returning to the their undeformed state when pressure is released, resulting in the creation of negative pressure in the chamber. For example, the walls of the standoff may be in the form of a bellows, suction cup or elastic ring.

Finally, rather than a single optical waveguide, the output surface of a first optical waveguide to which irradiation is initially applied may be mounted to a first surface of a second optical waveguide which also has a second skin-contacting surface opposite the first surface. Optical radiation received from the first waveguide is transmitted through the second waveguide to the skin-contacting surface thereof. The second skin-contacting surface of the second waveguide has a larger area than the output surface of the first waveguide and the second waveguide is formed to provide a larger optical aperture than of the first waveguide. The ratio of the spacing between the first and second surfaces of the second waveguide and a selected surface dimension of the skin-contacting surface of the second waveguide, for example the length of a side of the second surface or a diameter thereof, is approximately 1.5 to 1. Means may be provided for reflecting radiation back-scattered from the patient's skin into the second waveguide

back into the patient's skin. The means for reflecting may include forming at least a portion of the first surface and/or other surfaces of the second waveguide so as to reflect radiation impinging thereon, and such reflection from the second waveguide may also be made angle dependent.

The foregoing and other objects, features and advantages of the invention will be apparent from the following more particular description of preferred embodiments of the invention as illustrated in the accompanying drawings.

In the Drawings

Fig. 1 is a schematic semi-block diagram of a simplified EM radiation treatment system suitable for use in practicing the teachings of this invention.

Fig. 2 is a side sectional view of a head or applicator suitable for use in the system of Fig. 1 in accordance with teachings of this invention.

Fig. 3a is a graph illustrating a calculated relationship over time between the temperature at the waveguide at two Δd 's where a sensor may be located and the temperature at three different depths in a patient's skin, including at the DE or basal junction.

Fig. 3b is a graph illustrating a measured relationship over time between the temperature at the waveguide sensor for a preferred Δd and the temperature at two different depths in a patient's skin, including at the DE or basal junction.

Fig. 4 is a graph illustrating temperature sensor output over time for selected conditions.

Figs. 5a and 5b are simplified side sectional views of two alternative heads or applicators for providing a reflection aperture matching the aperture of radiation back-scatter.

Figs. 6a and 6b are simplified side sectional views of a head or applicator which utilizes negative pressure to draw a fold of skin into a cavity before negative pressure is applied and after negative pressure is applied respectively.

Figs. 7a and 7b are simplified side sectional views of a head or applicator for another embodiment of the invention which utilizes negative pressure to draw a fold of skin into a cavity at an intermediate step in the creation of the negative pressure and after negative pressure has been created respectively.

Figs. 8a, 8b and 8c are simplified side sectional views of a head or applicator for still another embodiment which uses negative pressure to draw a fold of skin into a chamber shown before negative pressure is created, at an intermediate stage in the creation of negative pressure and after negative pressure has been created respectively.

Fig. 9 is a simplified side sectional view of a head for an alternative embodiment of the invention which provides an expanded optical aperture for the head.

Fig. 10 is a simplified side sectional view of a head for an alternative embodiment which head is suitable for moving across a patient's skin during treatment.

5

Detailed Description

Fig. 1 is a simplified block diagram of a system 10 which may be utilized for treating a selected dermatological condition in accordance with the teachings of this invention. The system includes an electromagnetic (EM) radiation source 12 which is connected through a fiber optic
10 light pipe or other suitable optical conveyor 14 to an applicator or head 16, which head is in contact with the skin 18 of a patient. Controls 20 are provided which receive information from source 12 and head 16 and which control operation of the system in response to these inputs and others. EM source 12 may be a ruby laser, alexandrite laser, diode laser or other laser source providing radiation of a suitable wavelength for the laser treatment to be performed, or may be
15 a lamp or other non-coherent electromagnetic radiation source providing signals at the requisite wavelength. Particularly for non-coherent light sources, various techniques may be utilized to filter, frequency shift or otherwise control the output from the source to achieve radiation within a desired wavelength band. The radiation wavelength may be narrow band, down to a single wavelength, or wide band, and may vary over a wide spectrum from infrared through ultraviolet,
20 depending on the treatment to be performed and the radiation source utilized. Source 12 may be a pulsed source, either under operator control or at a fixed or controlled repetition rate, or may, as taught in copending applications Serial No. 09/078,055, be a continuous wave (CW) source. Controls 20 may be a suitably programmed general purpose or special purpose computer, may be hard wired circuitry, or may be a hybrid of special purpose circuitry and programmed
25 computer circuitry. Skin 18 has an epidermal layer 22, and a dermal layer 24, the junction of these two layers being sometimes referred to as the DE junction or basal layer 26.

Radiation from source 12 passes through head 16 and is emitted therefrom as a converging beam 28 which is applied to an area 30 in dermis 24 containing the element to be treated. Area 30 may, for example, contain a hair follicle which is to be destroyed in order to
30 achieve removal of unwanted hair, may be tattoo pigment which is to be removed, may be a spider vein or other blood vessel which is to be coagulated and removed or may be some other dermatological condition which is to be treated by the radiation. As discussed earlier, treatment

of a patient is complicated by the fact that there may be significant variations among patients, and in different areas of the body of the same patient, in the thickness of epidermal layer 22, in the pigmentation of this layer (and in particular in the quantity of melanin at DE junction 26), and in other characteristics of the skin. These variations make it difficult to achieve a desired therapeutic effect without potential damage to the area of the patient's epidermis overlying treatment area 30.

Fig. 2 illustrates a head 16 suitable for use in the system of Fig. 1. Referring to Fig. 2, head 16 includes a waveguide or lens 40 of an optically transparent material which also has good heat transfer properties and preferably provides a good index of refraction match with skin. Sapphire is a currently preferred material for the waveguide, although other materials could also be used. Waveguide 40 is supported by a holder ring 42 mounted in an exterior housing 44. A thermocouple, thermistor or other suitable temperature sensor 46 is mounted in contact with waveguide 40, between the waveguide and holder 42. The distance (Δd) of sensor 46 from the end of waveguide 40 in contact with the patient's skin is critical and, for reasons to be discussed later, should be no more than 5 mm. Δd is preferably in the 1-2 mm range, with approximately 1 mm being the currently preferred distance. While a single temperature sensor 46 is shown in Fig. 2, two or more such sensors spaced around waveguide 40 at the same distance Δd from the end of the waveguide may be preferable to average out temperature variations which may occur in the waveguide.

Thermoelectric cooling elements 48 are also provided in contact with waveguide 40. While two such elements are shown in Fig. 2, typically at least four such elements, substantially evenly spaced around the periphery of waveguide 40, would normally be provided. Thermoelectric elements 48 may for example be Peltier elements. Electrical connections are made to sensor(s) 46 and to thermoelectric elements 48 in a manner known in the art and to simplify the figure are not specifically shown therein.

The sides of thermoelectric elements 48 opposite those in contact with waveguide 40 are in thermal contact with heat sink or radiator 50 having channels 52 formed therein through which a cooling fluid such as air or water flows, the cooling fluid entering the head through a fluid junction 54 and exiting through a fluid junction 56 (or entering through fluid junction 56 and exiting through fluid junction 54).

Optical radiation is applied to the head through an optical fiber, fiber bundle or other light pipe 58 which terminates at a chamber 60. Radiation exiting optical fiber 58 expands in chamber

60 before entering waveguide 40 for application to the patient's skin. Fiber 58 is mounted in a sleeve 62 of optically opaque material, the rear portion of which is mounted in a tube 64 and the forward portion of which extends through a holder assembly 66. Tube 64 is mounted in a chamber 68 formed in the rear of holder assembly 66 to permit assembly 69, which includes fiber
5 58, sleeve 62 and tube 64, to be moved forward and backward, moving fiber 58 in chamber 60 to adjust the optical aperture of the head. O-rings 70 and 72 seal chamber 60 to keep air and moisture out so as to avoid condensation on cooled optical surfaces 74 and 76. Nitrogen or another gas which does not condense at temperatures down to -40°C is utilized to fill chamber 60.

10 Surface 74 of the waveguide is an optical reflecting surface as are all surfaces of chamber 60, including surface 76 at the rear thereof. As will be discussed later, these surfaces retroreflect back-scattered light from the patient's skin. The side walls of both waveguide 40 and chamber 60 may also be fully reflective or may selectively reflect in a manner and for reasons to be discussed later.

15 In operation, assembly 69 is initially positioned to achieve a desired optical aperture for head 16. Thermoelectric elements 48 are also energized to cool waveguide 40 to a selected temperature, for example 10°C to -40°C . The criteria is to bring the waveguide 40 to a sufficiently low temperature to achieve the desired cooling of epidermis 22 without resulting in tissue temperature being brought down to a level where water in the cells might freeze. Good
20 results have been achieved with a waveguide temperature in the 0°C to -30°C range, with a preferred temperature of approximately -10°C .

When the above preliminary steps have been completed, head 16 may be brought into physical contact with an area of the patient's skin where treatment is to be performed. This contact may be under low pressure, preferably at least sufficient to establish good thermal contact
25 between waveguide 40 and the patient's skin, where the objective is to coagulate blood in for example a spider vein, leg vein or other vein or blood vessel, or may be under pressure greater than the patient's blood pressure for hair removal or other applications where it is preferable to remove blood from the region of skin between waveguide 40 and area 30 under treatment.

In any event, head 16, and in particular waveguide 40 thereof, should be placed in contact
30 with the patient's skin with sufficient pressure to assure good thermal contact between the patient's skin and waveguide 40. In accordance with the teachings of this invention, the fact that such good thermal contact has been established can be detected through use of sensor 46. In

particular, as seen in Figs. 3a and 3b, with the sensor positioned approximately 1 mm from the contact surface of waveguide 40, (i.e. $\Delta d = 1$ mm), the temperature at the sensor has a profile 90 in Fig. 3a and 90' in Fig. 3b which increases sharply for the first quarter to one-half second after such thermal contact has been established. The reason for this is that the waveguide is acting as a heat sink for the patient's skin during this time interval and the heating of the waveguide at the skin-contacting end thereof is greater than the cooling effect of thermoelectric device 48 at this surface (i.e. there is a small temperature gradient across waveguide 40). The detection of the temperature profile 90, 90' by sensor(s) 46 can be interpreted by controls 20 as an indication of good thermal contact between the waveguide and the patient's skin. If such a thermal profile is not detected, controls 20 inhibit the activation of radiation source 12 and/or prevent radiation from the source being applied to head 16. This assures that radiation is not delivered to the skin unless the epidermis has been adequately cooled to prevent thermal damage thereto.

Referring for example to Fig. 3a, it is seen that the placement of sensor 46 relative to the skin-contacting surface of waveguide 40, or in other words the distance Δd , is critical in order to achieve this objective. In particular, while profile 90 is achieved for a Δd of approximately 1.2 mm, profile 91, which is achieved with a Δd of approximately 4.8 mm, evidences far less sensitivity to temperature changes at the DE junction and is therefore not particularly useful in assuring good thermal contact between the waveguide and the patient's skin. Actual profile 90' (Fig. 3b), while slightly more stepped and less smooth than the theoretical profile 90 of Fig. 3a, is sufficiently similar to this profile so as to permit easy identification of good thermal contact. Differences between Figs. 3a and 3b may also arise from the fact that the waveguide in Fig. 3a starts at a temperature of -10°C while the waveguide in Fig. 3b starts at a temperature of approximately -27°C .

Referring again to the Figures, and in particular to Fig. 3a, it is seen that a major portion of the waveguide cooling occurs within a period of between 0.5 and 2 seconds from full contact, the time varying somewhat with the initial temperature of the waveguide and the desired final temperature at the DE junction. Therefore, assuming good thermal contact has been made, an operator may operate source 12 some predetermined time after making contact with the patient's skin, for example a half second thereafter, but not more than approximately 2 seconds thereafter, to avoid significant cooling of the dermis.

However, since cooling of the skin may vary depending on a number of factors, including variations in the equipment being utilized, the color and nature of the patient's skin, the thickness

of the patient's skin and the like, it is preferable that the temperature at the DE junction be measured and that the radiation source 12 be operated as soon as this temperature has dropped to a desired level. As can be seen from Figs. 3a and 3b, the temperature profile 90 at sensor 46 tracks the temperature profile 92 at the DE junction as does the temperature profile 90' for DE junction temperature profile 92'. Thus, the output from sensor 46 can be utilized by control 20 as an indication of temperature at the DE junction, and radiation source 12 can be operated by control 20 when this temperature reaches a predetermined value. This assures that radiation is not applied to the patient until the patient's epidermis has been fully cooled to the desired level and that the operation of laser source 12 is not delayed so long as to cause cooling of portions of the follicle which are to be destroyed. In particular, 94 is a profile taken approximately 1 mm from the surface of the patient's skin, which is approximately the depth of the bulge in a hair follicle, and may be a depth where other dermatological treatments such as tattoo removal, treatment of port wine stain or vascular lesions may occur. From Fig. 3a it is seen that for a time over two seconds, there is a significant drop in temperature at this depth, which can be 10°C or more. For many dermatological applications, such a drop in temperature 1 mm into the dermis is undesirable, and in particular can adversely affect the desired treatment. Curves 96, 96' are temperature profiles with time deeper into the dermis, for example 2 mm therein. At this depth, the cooling effect of cooled waveguide 40 is not significant, perhaps a few degrees Celsius. This lack of cooling effect at deeper depths stems both from the greater distance of these point from the cooling source and from the proximity of tissue at this depth to the warming effect of blood-carrying vessels. The teachings of this invention thus permit and assure that the radiation source is not operated to cause heating of the patient's epidermis until the epidermis has been cooled to the desired depth and temperature, but that firing of the radiation source occurs before there is any significant cooling of the dermis. The invention further permits these controls to be performed completely automatically, thereby reducing the skill level required to safely perform such dermatological procedures, and permitting such procedures to be performed by less skilled and therefore less expensive personnel.

During the firing of the radiation source, control 20 continues to monitor the temperature at sensor 46. If at any time during the firing of the radiation source, there is an increase in temperature at sensor 46 which deviates from what would be anticipated from profile 90, controls 20 can immediately turn off the source 12 to prevent any thermal damage to the patient's epidermis 22.

While for certain treatments, the system of this invention may be able to detect successful completion of the treatment, this is not easy to do, particularly for treatments being performed several millimeters into the dermis. The radiation source is therefore typically fired for a predetermined time interval and/or head 16 is maintained in contact with the patient's skin for a predetermined time interval. Control 20 may determine when such time interval has expired, turn off source 12 when such time period has passed and perhaps generate an audio or visual indication to the operator to remove head 16 from the patient's skin. These steps also reduce the skill level required for using the system.

As indicated earlier, one problem with utilizing radiation to treat dermatological conditions is that a significant portion of the radiation applied to the patient's skin is back-scattered and lost, therefore increasing the power required from the radiation source utilized, and thus the cost of the system. One solution to this problem is to efficiently collect radiation back-scattered from the patient's skin and to reflect such radiation back into the patient's skin with minimum loss. Fig. 2 shows a retroreflector which is particularly well suited for performing this function. In particular, waveguide 40 has an aperture which is larger than the optical aperture of the radiation applied to the patient's skin and which is instead substantially equal to the aperture of radiation back-scattered from the patient's skin. Thus, substantially all of the back-scattered radiation is collected in waveguide 40. Waveguide 40 has an external coating or is otherwise designed in manners known in the art so as to totally internally reflect the back-scattered radiation collected therein. Some of such radiation impinges on reflecting surface 74 and is returned through the totally internally reflecting waveguide from such surface to the patient's skin. The remainder of the back-scattered radiation extends into chamber 60 which is also totally internally reflected and ultimately impinges on reflecting surface 76 which returns this radiation with minimal loss to the patient's skin. Thus, the retroreflective design for the head 16 in Fig. 2 results in the collection and retroreflection back into the skin of substantially all back-scattered radiation.

In the discussion above, the side walls and back walls of both waveguide 40 and chamber 60 are fully reflecting so that substantially all of the light retroreflected into waveguide 40 is returned to the patient's skin. However, since radiation entering the waveguide from the skin (before refraction on entering the waveguide), is retroreflected back into the patient's skin at substantially the same angle, such radiation at relatively sharp angles, (i.e., at angles more nearly parallel to the patient's skin than perpendicular) contributes primarily to heating the patient's epidermis, potentially causing thermal damage thereto, without reaching region 30, and therefore

without having any therapeutic effect. It is therefore preferable that such sharply angled radiation not be retroreflected or that, as a minimum, the retroreflection of such radiation be substantially attenuated. This can be accomplished in the embodiment of Fig. 2 by for example utilizing an angle dependent coating for the side walls of waveguide 40, the rear wall of waveguide 40, or both so that these walls of the waveguide either do not reflect or minimally reflect large angle radiation entering the waveguide, while more strongly reflecting radiation coming in at a more closely perpendicular angle. Alternatively, the side wall may have varying coefficients of reflection, being less reflective for the portions of the wall closest to the tip or skin contacting surface of waveguide 40 and more reflective toward the rear of the waveguide. Other techniques could also be utilized to assure that waveguide 40 and chamber 60 more strongly reflect retroreflected radiation applied thereto at an angle more nearly perpendicular to the skin surface than radiation applied thereto at an angle more nearly parallel to the skin surface, the perpendicular radiation being substantially fully retroreflected, while the parallel radiation is substantially attenuated.

Fig. 4 illustrates the voltage output at sensor 46 as a function of time under selected operating conditions. The solid line 93 illustrates a representative output when the waveguide 40 of head 16 is placed in contact with a patient's skin at time t_1 . From time t_1 to time t_2 the temperature at the sensor increases as the skin in contact with waveguide 40 is cooled. At time t_2 , source 12 is operating to apply a radiation pulse through the waveguide to the patient's skin causing an increase in the temperature of the patient's skin which is reflected as a spike in the voltage output from the temperature sensor 46. The temperature then decreases rapidly until just before a time t_3 when backscattered radiation from the patient's skin starts to be received in the waveguide. The time between t_2 and t_3 is a function of the thickness of the patient's epidermis to the DE junction where melanin is being heated and the amplitude of the spike at time t_3 is a function the patient's skin type, more energy being reflected for a patient having darker skin, for example spike 95, than for patients having lighter skin. Thus, the amplitude of the spike which occurs at time t_3 may be utilized as an indication of the patient's skin type, and this information may be reviewed at least periodically by the system controls, since skin type will vary even for a given patient as different areas of the patient's skin are being treated.

Patient's skin type may also be determined by taking two successive readings, one with head 16 not in contact with the patient's skin and a second with the head in contact with the patient's skin. Curve 93 is an example of the output which is obtained when the head is in

contact with the patient's skin, while curve 97 which would start at time t_2 , is indicative of an output which would be obtained when the laser is fired at time t_2 with the head not in contact with the patient's skin. Since the output in air is proportional to the coefficient of absorption for air times the applied laser energy ($V_A=k_0E$) and V_s when the head is in contact with the patient's skin

5 is given by

$$V_s = k_0 E + k_0 R E$$

where R is the coefficient of reflection from the patient's skin, $R=(V_s-V_A/k_0E)$. Since k_0 and E are known values, the difference in voltage for the two readings provides a reliable indication of the coefficient of reflection from the patient's skin in the area under treatment, or in other words of the patient's skin type. The output from temperature sensor 46 may also be utilized for other

10 purposes.

Fig. 5a shows an alternative embodiment of the invention for performing the retroreflector function where the surface area or aperture of waveguide 40 is substantially equal to the optical aperture of radiation applied to the patient's skin. It is therefore smaller than the aperture D of radiation back-scattered from the patient's skin. Therefore, a reflector plate 97 is provided, which

15 may be a specular or diffuse reflector. Plate 97 has a hole which is sized and shaped to permit waveguide 40 to fit therein. Plate 97 may, for example, extend for approximately 1 to 6 millimeters on either side of waveguide 40, but this dimension will vary with application, and can be outside the above range for selected applications. The reflective effect can be enhanced by providing a liquid or other reflective index-matching substance 98 between the skin 18 and

20 the waveguide 40/plate 97, which substance has a reflective index equal or greater than the reflective index of the skin. This decreases the total internal reflection from the skin surface, allowing better return of radiation into the deep layers of skin by reflector 97. Thermoelectric elements 99 in contact with reflective plate 97, which may be formed of a material having good thermal conducting properties such as metal, can be utilized to heat plate 97 to a temperature of,

25 for example, 45-50 C°. Plate 97 can thus preheat the area of the patient's skin surrounding the area where radiation is to be applied, thereby increasing the temperature at the treatment area in the dermis, and thus decreasing the light energy required for performing the desired treatment.

Fig. 5b illustrates an alternative embodiment wherein the reflector 97' has an enhanced efficiency by being formed in a cone or other concave shape. This results in the back-scattered

30 light reflected into the skin being concentrated in the region of the radiation or collimated beam

delivered into the skin through waveguide 40, thus increasing the quantity of radiation delivered to the treatment area. Except for the shape of the reflection plate 97', the embodiment of Fig. 5b otherwise functions in the same way as the embodiment of Fig. 5a. As for the embodiment of Fig. 2, retroreflection from waveguide 40 can be angle dependent for the embodiments of Fig. 5a and 5b and, particularly for the embodiment of Fig. 5a, reflection from plate 97 can also be made angle dependent by suitably coating the reflecting surface thereof.

Fig. 6a and 6b show another embodiment of the invention which differs from those previously described in that reflection plate 97" is even more angled than for the embodiment of Fig. 5 and is generally in the form of a truncated cone which is secured to the lower end of waveguide 40 in a manner so as to form a substantially air-tight seal therewith. Such securing may be by providing a pressure fit between plate 97" and waveguide 40, but is preferably achieved by applying a suitable adhesive between the two components. Another alternative would be to have some form of screw thread formed in or on waveguide 40 which mates with a corresponding tread on plate 97", but such tread might interfere with the optical properties of waveguide 40. A hose 100 passes between plate 97" and waveguide 40 and is sealed therebetween, hose 100 being attached to a source of negative pressure (for example vacuum pressure) (not shown). As may be best seen in Fig. 6a, when head 16 of this embodiment is pressed against skin 16, a chamber 99 is formed which is defined by the light reflecting walls of plate 97", the lower surface of waveguide 40, and the surface of the patient's skin 18 which is inside the cone of plate 97". Plate 97" will sometimes also be referred to hereinafter as a standoff.

In operation, once head 16 is in the position shown in Fig. 6a, vacuum is applied through hose 100 to chamber 99 to remove air therefrom. This has the effect of drawing a portion or fold 105 of the patient's skin into chamber 99 and into contact with the lower skin-contacting surface of waveguide 40. This can reduce the distance between waveguide 40 and the target volume in skin portion 105 at which treatment is desired and also brings this target volume into chamber 60 where back-scattered radiation retroreflected from the reflecting walls of plate 97" concentrate this radiation on the target volume. This reduces the amount of energy required from EM source 12 and significantly enhances the overall efficiency of the system. The depth of chamber 99 from the bottom of waveguide 40 to the skin surface would typically be in the 5 mm range and should normally not be more than approximately 10 mm. The diameter D of standoff or plate 97" at the skin-contacting end thereof is, as for the embodiment of Figs. 5a and 5b substantially equal to the aperture of back-scatter radiation.

Fig. 7 shows and embodiment of the invention which differs from that shown in Fig. 6 in that, instead of a vacuum line 100 being utilized to obtain reduced or vacuum pressure in chamber 99, standoff 101 is in the form of a bellows which collapses when head 16 is pressed against the skin as shown in Fig. 7a forcing air out of chamber 99. When pressure on head 16 is removed, or if slight upward pressure is applied to the head, bellows 101 straightens as shown in Fig. 7b. The vacuum in chamber 99 holds bellows 101 against the skin resulting in skin fold 105 again being drawn into chamber 99 as bellows 101 returns to its normal position. The embodiment of Fig. 7 functions substantially the same as the embodiment of Fig. 6 with the inside of bellows 101 having a reflective coating or otherwise being reflective. While the base of bellows or standoff 101 has only a slightly larger aperture than the aperture d of waveguide 40, this is not a problem since substantially all of the back-scattered radiation from the skin is emitted into chamber 99 where it is reflected in a concentrated manner back to the target volume and there should be virtually no back-scattered radiation outside of chamber 99. Sharply angled radiation is also productively utilized for these embodiments. An effect substantially the same as that of Fig. 7 can be achieved by using a standoff in the form of a suction cup in lieu of the standoff's 97" or 101 as shown.

Figs. 8a-8c shows still another embodiment of the invention which differs from that shown in Fig. 7 in that a ring 102 of an elastic material is substituted for the bellows 101. When ring 102 is pressed against the skin as shown in Fig. 8b, the ring deforms permitting waveguide 40 to move substantially into contact with skin 18 as air is forced out of chamber 99. When the pressure is released, elastic ring 102 returns to the condition shown in Fig. 8c, resulting in skin fold 105 being drawn into the chamber as shown.

While three standoff configurations have been shown and/or described above for achieving vacuum pressure, or at least negative pressure, in chamber 99 by collapsing a standoff and then permitting it to return to its normal position, the embodiments shown and/or described are by way of illustration only, and other standoff configurations for achieving the same objective might also be utilized. Further, in addition to the use of vacuum hose 100 as shown in Fig. 6, other methods known in the art may be used for achieving the desired reduced pressure in chambers 99 so as to cause a fold of skin 105 to be drawn therein for irradiation.

Fig. 9 shows still another embodiment of the invention which differs from those previously shown in that, rather than a bottom surface of waveguide 40 being in contact with the patient's skin 18, the lower end of waveguide 40 is in contact with a second waveguide 103 which

is preferably of sapphire or other material having good optical and thermal conduction properties. Sapphire is particularly preferred, because it also provides a fairly good optical index match with skin. Index matching material 98 may be utilized between waveguide 103 and the patient's skin to further enhance this match. While not specifically shown in Fig. 9, waveguide 103 would also have, for preferred embodiments, one or more temperature sensors 46 positioned close to its skin-contacting surface and one or more thermoelectric elements 48 or other temperature control elements in contact therewith to preheat and/or cool the patient's skin 18 as required. A reflective coating 104 may also be provided on the rear surface of waveguide 103 to, in conjunction with the retroreflector previously described for waveguide 40, retroreflect substantially all radiation back-scattered from the patient's skin. Angle dependent retroreflection might also be employed for this embodiment using techniques previously discussed, such angle dependent retroreflection occurring at least for waveguide 103, and preferably for both waveguides. The advantage of the embodiment shown in Fig. 9 is that it significantly enlarges the optical aperture for treatment, permitting treatment over a relatively large area, for example hair removal over a patient's legs or back, to be accomplished far more rapidly than when a head having a smaller aperture is utilized. The skin-contacting surface of waveguide 103 may have a variety of shapes, and may for example be circular or square. A circular waveguide 103 might for example have a diameter of approximately 1 inch while a square waveguide 103 might have sides 2 cm long, the height of waveguide 103 preferable being roughly 1.5 times this dimension. These dimensions are, however, being provided by way of illustration only and the specific dimensions of waveguide 103 will vary with application.

In the discussion to this point, it has been assumed that the head utilized is applied to a point on a patient's skin where treatment is to be performed and that, after a suitable period of time has passed for cooling of the skin to the DE junction to have occurred, an optical radiation pulse, for example a laser pulse, is applied through the waveguide to treatment area 30. Fig. 10 shows an embodiment of the invention which, like the embodiments taught in application Serial No. 09/078,055, is intended to be in contact with the patient's skin 18 and to be moved in direction 112 over the skin while remaining in contact therewith. Radiation applied to waveguides light paths 114 in this head may be continuous wave or may be pulsed at a high enough rate to permit movement of the head over the treatment area. For the embodiment shown in Fig. 10, the head has an area 116 ahead of waveguides 114 which passes over the treatment area before radiation is applied thereto. Region 116 is preferably of a thermally conductive

material and is insulated from a second region 118 of the head, which is preferably also of a thermally conductive material, by a thermally insulating layer 120. A thermal electric element or other suitable heater/chiller 122 is in contact with portion 116 and may be used to either preheat or precool the treatment area. For example, if element 122 is a heater, it can heat the skin
5 down to region 30 to a temperature below that at which thermal damage would occur. Further, a temperature sensor 124 is provided, for example up to 5 mm from the skin contacting surface (and preferably less, i.e., to 1 to 2 mm) to indicate skin temperature at for example the DE junction. Sensor 124, by detecting the heating of melanin in the epidermis provides an indication of skin type for the patient, which indication can be used to control the radiation applied. It also
10 assures that overheating in the epidermis does not occur. A thermal electric element or other suitable cooler 126 connected to region 118 cools the epidermis ahead of waveguides 114 coming over a treatment area. A temperature sensor 128 can also be provided in region 118, for example up to 5 mm from the skin contacting surface, to assure that this region has cooled sufficiently before radiation is applied thereto and to protect against thermal damage to this region. While
15 a single pair of waveguides 114 are shown in Fig. 10, typically a plurality of such waveguides would be stacked adjacent to each other in a direction into the figure. Two or more heaters/chillers 122, 126 could also be provided and two or more sensors 124, 128 could also be provided. Further, the sensor technology of this invention could also be utilized with other ones of the embodiments shown in application Serial No. 09/078,055.

20 While the invention has been described above with reference to a particular system 10 and to particular head designs 16, neither are limitations on the invention. In particular, other techniques known in the art, for example circulating water or air, could be utilized for cooling waveguide 40 in lieu of thermoelectronic cooling elements 48, although such thermoelectronic cooling elements are at this time preferred. Some elements 48 (or other thermal control elements)
25 might also be used to heat waveguide 40 to preheat the target area, after which either the same or different thermal control elements would be used to cool the waveguide as previously indicated to cool the patient's epidermis in the treatment area. A lens may also be substituted for waveguide 40, although waveguide 40 is currently preferred because of its superior thermal properties and its superior performance in retroreflection. Other light guiding/transmitting
30 element may also be used and, in some applications, two or more such elements may be used as shown in Fig. 10, rather than a single element to transmit EM radiation through the head to the patient's skin. Other details of construction for head 16 or head 110 may also be varied,

depending on application. Thus, while the invention has been particularly shown and described above with reference to preferred embodiments, the foregoing and other changes in form and detail may be made therein by one skilled in the art while still remaining within spirit and scope of the invention which is to be defined only by the appended claims.

Claims

1. A head for applying EM radiation of a wavelength appropriate for treating a selected patient dermatologic problem to a selected volume of a patient's skin, the volume containing the
5 problem to be treated, the head including:
an optical waveguide;
a light path for directing the EM radiation to a first end of the waveguide, said waveguide having a skin-contacting second end which is opposite said first end; and
a sensor at said second end of the waveguide which senses the temperature thereat.
10
2. A head as claimed in claim 1 wherein said sensor is located no more than a few millimeters from the second end of the waveguide.
3. A head as claimed in claim 2 wherein said sensor is located within 5 millimeters of said
15 second end of the waveguide.
4. A head as claimed in claim 2 wherein said sensor is located within 2 millimeters of said second end of the waveguide.
- 20 5. A head as claimed in claim 2 wherein said sensor is located within 1 millimeter of said second end of the waveguide.
6. A head as claimed in claim 1 including a mechanism for removing heat from the waveguide.
25
7. A head as claimed in claim 6 wherein said mechanism includes a thermoelectric device having one side in thermal contact with said waveguide and an opposite side in thermal contact with a temperature sink.
- 30 8. A head as claimed in claim 1 wherein said head has a reflection aperture at a skin-contacting end thereof at least substantially as great as the aperture of radiation back-scattered from the patient's skin.

9. A head as claimed in claim 8 wherein said second end of the waveguide has an aperture at least substantially as great as the aperture of radiation back-scattered from the patient's skin.

10. A head as claimed in claim 8 wherein at least part of the back-scattered radiation enters
5 said waveguide and is substantially internally reflected within said waveguide; and
including a reflector within said waveguide for returning back-scattered radiation through the waveguide to the patient's skin.

11. A head as claimed in claim 10 wherein said reflector is at said first end of the waveguide.

12. A head as claimed in claim 11 wherein said reflector is also along at least a portion of waveguide sidewalls, and wherein said reflector has a coefficient of reflection at areas thereof such that backscattered radiation at angles nearer perpendicular to said skin contacting second end are reflected more strongly than back scattered radiation at angles nearer parallel to said
15 second end.

13. A head as claimed in claim 8 including a reflector plate surrounding said waveguide at the second end thereof, the combined area of the plate and the waveguide projecting therethrough being substantially equal to the aperture of radiation back-scatter.

14. A head as claimed in claim 13 wherein said plate has a concave shape.

15. A head as claimed in claim 13 including a means for controlling the temperature of the plate.

16. A system for treating a selected dermatologic problem located in a selected volume of a patient's skin at a depth d , which depth is below the DE junction, comprising:

a source of EM radiation of a wavelength appropriate for treating said problem;

an optical waveguide having a first end at which said radiation is applied and a second
30 end for contacting the patient's skin, which second end is opposite said first end;

a temperature sensor at said second end of the waveguide, the temperature at said sensor being indicative of the temperature at a selected depth within the patient's skin;

a mechanism which removes heat from the patient's skin at least in the area thereof in contact with said waveguide; and

controls operative in response to said sensor indicating that the patient's skin at said selected depth has been cooled to at least a selected temperature for permitting radiation from said source to be passed through said waveguide to the patient's skin, including said selected volume.

17. A system as claimed in claim 16 wherein said mechanism removes heat from the waveguide, the waveguide, when in contact with the skin, removing heat from, and thus cooling, the skin.

18. A system as claimed in claim 17 wherein said selected depth is the DE junction, and wherein said controls are operative in responsive to said sensor for maintaining the DE junction within a selected temperature range during application of said radiation to the patient's skin.

19. A system as claimed in claim 17 wherein said controls detect a temperature profile at said sensor, said profile being indicative of contact of said waveguide with the patient's skin, and wherein said controls prevent said radiation from passing to the patient's skin unless a predetermined profile is detected.

20. A system as claimed in claim 17 wherein said controls operate said mechanism to cool said waveguide to a desired temperature, and wherein said controls are responsive to said sensor for determining when said temperature has been reached.

21. A system as claimed in claim 16 wherein said sensor is located no more than a few millimeters from the second end of said waveguide.

22. A system as claimed in claim 16 wherein said second end of the waveguide has an aperture at least substantially as great as the aperture of radiation back-scattered from the patient's skin.

23. A system as claimed in claim 22 wherein back-scattered radiation is substantially internally reflected within said waveguide; and

including a reflector within said waveguide for returning back-scattered radiation through the waveguide to the patient's skin.

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24. A system as claimed in claim 23 wherein said reflector is at said first end of the waveguide.

25. A system as claimed in claim 24 wherein said reflector is also along at least a portion of waveguide sidewalls, and wherein said reflector has a coefficient of reflection at areas thereof such that backscattered radiation at angles nearer perpendicular to said skin contacting second end are reflected more strongly than back scattered radiation at angles nearer parallel to said second end.

15 26. A system for treating a selected dermatologic problem located in a selected volume of a patient's skin at a depth d, which depth is below the DE junction, comprising:

a source of EM radiation of a wavelength appropriate for treating said problem;

an optical waveguide having a first end at which said radiation is applied and a second end for contacting the patient's skin, which second end is opposite said first end;

20 a mechanism which cools the patient's skin, at least in the portion thereof in contact with said waveguide, when said second end is in contact with the patient's skin;

a temperature sensor at said second end of the waveguide, the temperature at said sensor being indicative of the temperature at the patient's DE junction; and

25 controls operative in response to the sensor sensing a selected increasing temperature profile at the sensor when the waveguide is placed in contact with the patient's skin for permitting radiation from said source to be passed through said waveguide to the patient's skin, including said selected volume.

27. A system as for treating a selected dermatologic problem located in a selected volume of a patient's skin, comprising:

a source of EM radiation of a wavelength appropriate for treating said problem;

an optical waveguide having a first end at which said radiation is applied and a second end for contacting the patient's skin, which second end is opposite said first end;

controls for selectively permitting radiation from said source to be passed through said waveguide to the patient's skin, including said selected volume;

5 said second end of the waveguide having an aperture at least substantially as great as the aperture of radiation back-scattered from the patient's skin, the back-scattered radiation being substantially internally reflected within said waveguide; and

a reflector within said waveguide for returning back-scattered radiation through the waveguide to the patient's skin.

10

28. A system as claimed in claim 27 wherein said reflector is at said first end of the waveguide.

29. A system as claimed in claim 28 wherein said reflector is also along at least a portion of
15 waveguide sidewalls, and wherein said reflector has a coefficient of reflection at areas thereof such that backscattered radiation at angles nearer perpendicular to said skin contacting second end are reflected more strongly than back scattered radiation at angles nearer parallel to said second end.

20 30. A head for applying EM radiation of a wavelength appropriate for treating a selected patient dermatologic problem at a selected volume of a patient's skin, the head comprising:

an optical waveguide;

a light path for directing the EM radiation to a first end of the waveguide, said waveguide having a skin-contacting second end which is opposite said first end;

25 some of the radiation passing through the waveguide to a patient's skin being back-scattered over a back-scatter aperture, said second end of the waveguide being at least part of a reflection aperture at least substantially as great as said back-scatter aperture, back-scattered radiation entering the waveguide being substantially internally reflected within said waveguide; and

30 a reflector within said waveguide for returning the back-scattered radiation entering the waveguide through the waveguide to the patient's skin.

31. A head as claimed in claim 30 wherein said reflector is at said first end of the waveguide.

32. A head as claimed in claim 31 wherein said reflector is also along at least a portion of waveguide sidewalls, and wherein said reflector has a coefficient of reflection at areas thereof such that backscattered radiation entering the waveguide at angles nearer perpendicular to said skin contacting second end are reflected more strongly than back scattered radiation entering at angles nearer parallel to said second end.

33. A head as claimed in claim 30 wherein said waveguide is cooled, and means for maintaining a moisture-free environment for said reflector to inhibit condensation thereon.

34. A head as claimed in claim 30 wherein said second end of the waveguide has an aperture at least substantially as great as the aperture of radiation back-scattered from the patient's skin.

35. A head as claimed in claim 30 including a reflector plate surrounding said waveguide at the second end thereof, the combined area of the plate and the waveguide projecting therethrough being substantially equal to the aperture of radiation back-scatter.

36. A head as claimed in claim 35 wherein said plate has a concave shape.

37. A head as claimed in claim 35 including a means for controlling the temperature of the plate.

38. A head for applying EM radiation of a wavelength appropriate for treating a selected patient dermatologic problem at a selected volume of a patient's skin, the head comprising:

a skin-contacting surface;

at least one light path passing through said head and terminating at said skin-contacting surface, said EM radiation being applied through said at least one light path to the patient's skin;

some of the radiation passing through the waveguide to a patient's skin being back-scattered over a back-scatter aperture, said head including reflection means for returning back-scattered radiation to the patient's skin, said reflection means having a reflection aperture at least substantially as great as said back-scatter aperture.

39. A head as claimed in claim 38 wherein said reflection means includes at least a portion of said skin-contacting surface being formed as a reflection plate.

40. A head as claimed in claim 39 wherein some of the back-scattered radiation enters said light path, and wherein said reflection means includes at least one reflection surface for the back-scattered radiation entering the light path.

41. A head as claimed in claim 40 wherein at least a part of said at least one reflection surface is in said light path.

42. A head for applying EM radiation of a wavelength appropriate for treating a selected patient dermatologic problem at a selected volume of a patient's skin, the head comprising:

at least on optical waveguide for receiving said EM radiation and for directing it to a skin-contacting surface of the at least one waveguide;

a standoff having a first and second end, the first end surrounding said at least one waveguide at its lower end and forming a substantially air-tight seal therewith, and said second end being adapted to contact the patient's skin over said selected volume to form a chamber between said skin-contacting waveguide surface, the patient's skin and walls of the standoff;

and means for creating negative pressure in said chamber to draw the patient's skin therein

and into contact with said skin-contacting surface.

43. A head as claimed in claim 42 wherein the walls of said standoff are reflective to return back-scattered radiation to the patient's skin.

44. A head as claimed in claim 42 wherein said means for creating negative pressure includes a hose mounted at one end to open into said chamber and connected at its other end to a source of negative pressure.

45. A head as claimed in claim 42 wherein said means for creating negative pressure includes the walls of said standoff being deformable when pressure is applied to the waveguide to permit the skin-contacting surface of the waveguide to contact the patient's skin, forcing most of the air

from said chamber, said walls returning to their undeformed state when pressure is released resulting in the creation of negative pressure in said chamber.

46. A head as claimed in claim 45 wherein said walls of the standoff are in the form of a bellows.

47. A head as claimed in claim 45 wherein said walls of the standoff are in the form of a suction cup.

48. A head as claimed in claim 45 wherein said walls of the standoff are in the form of an elastic ring.

49. A head for applying EM radiation of a wavelength appropriate for treating a selected patient dermatologic problem at a selected volume of a patient's skin, the head comprising:

at least one first optical waveguide for receiving said EM radiation and for directing it to an output surface of the at least one waveguide; and

a second optical waveguide having a first surface mounted to the output surface of the first optical waveguide to receive said EM radiation therefrom and having a second skin-contacting surface opposite said first surface, said skin-contacting surface having a larger area than said output surface and said second waveguide being formed to provide a larger optical aperture than that of said first waveguide.

50. A head as claimed in claim 49 wherein the ratio of the spacing between said first and second surfaces of the second waveguide and a selected surface dimension of said second surface is approximately 1.5 to 1.0.

51. A head as claimed in claim 50 wherein said selected surface dimension is one of the length of a side of said second surface and a diameter of said second surface.

52. A head as claimed in claim 49 including means for reflecting radiation back-scattered from the patient's skin into said second waveguide back into the patient's skin.

53. A head as claimed in claim 52 wherein said means for reflecting including forming at last a portion of said first surface so as to reflect radiation impinging thereon.

54. A head as claimed in claim 53 wherein said reflector is also along at least a portion of waveguide sidewalls, and wherein said reflector has a coefficient of reflection at areas thereof such that backscattered radiation entering the waveguide at angles nearer perpendicular to said skin contacting surface are reflected more strongly than back scattered radiation entering at angles nearer parallel to said skin contacting surface.

55. A head for applying EM radiation of a wavelength appropriate for treating a selected patient dermatologic problem at a selected volume of a patient's skin, the head comprising:

a skin-contacting surface;

at least one light path passing through said head and terminating at said skin-contacting surface, said EM radiation being applied through said at least one light path to the patient's skin;

and

a temperature sensor located in said head within a few millimeters of said skin contacting surface.

56. A head as claimed in claim 55 wherein said temperature sensor is located within 5 mm of said skin contacting surface.

57. A head as claimed in claim 55 wherein said head is moved across a patient's skin during treatment, and including a head portion of a thermally conductive material passing over the skin prior to said at least one light path, a said temperature sensor being located in said head portion.

58. A head as claimed in claim 57 including means for one of heating and cooling said head portion to preheat/precool the patient skin prior to application of EM radiation thereto.

59. A head as claimed in claim 57 including means for heating said head portion to preheat the patients skin prior to application of EM radiation thereto, and means for utilizing the output of said temperature sensor in response to the preheating to determine patient skin type.

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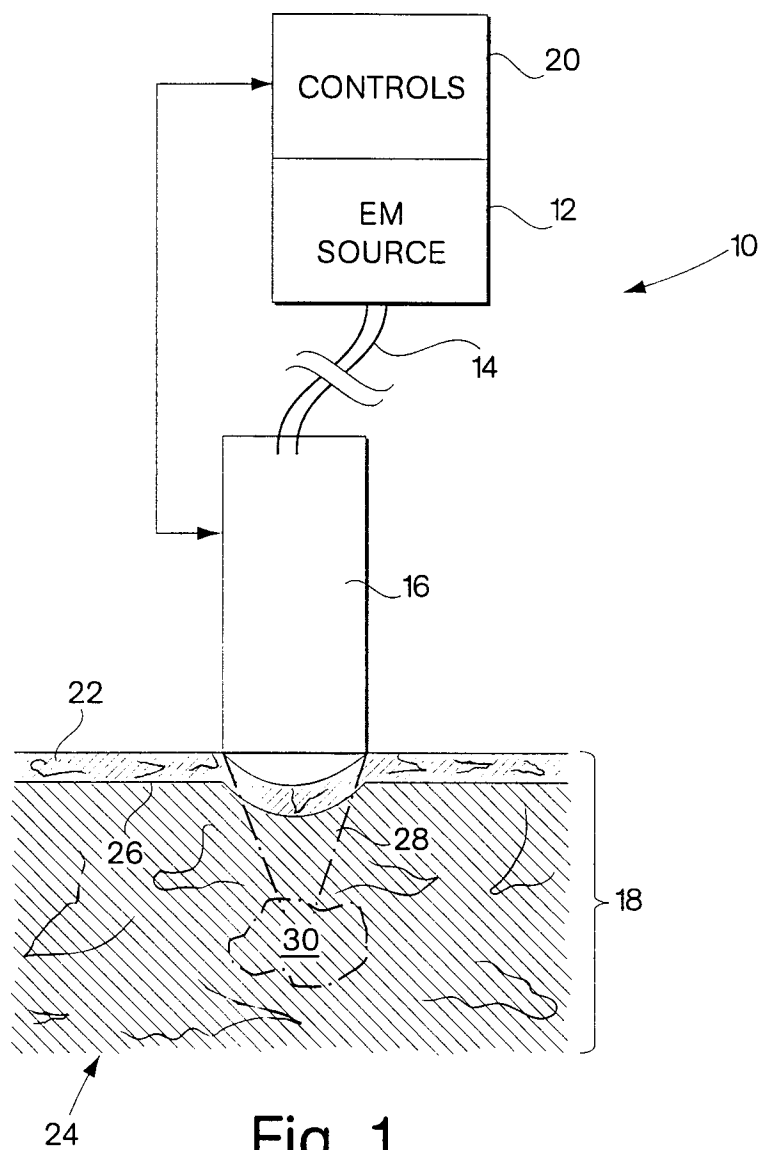
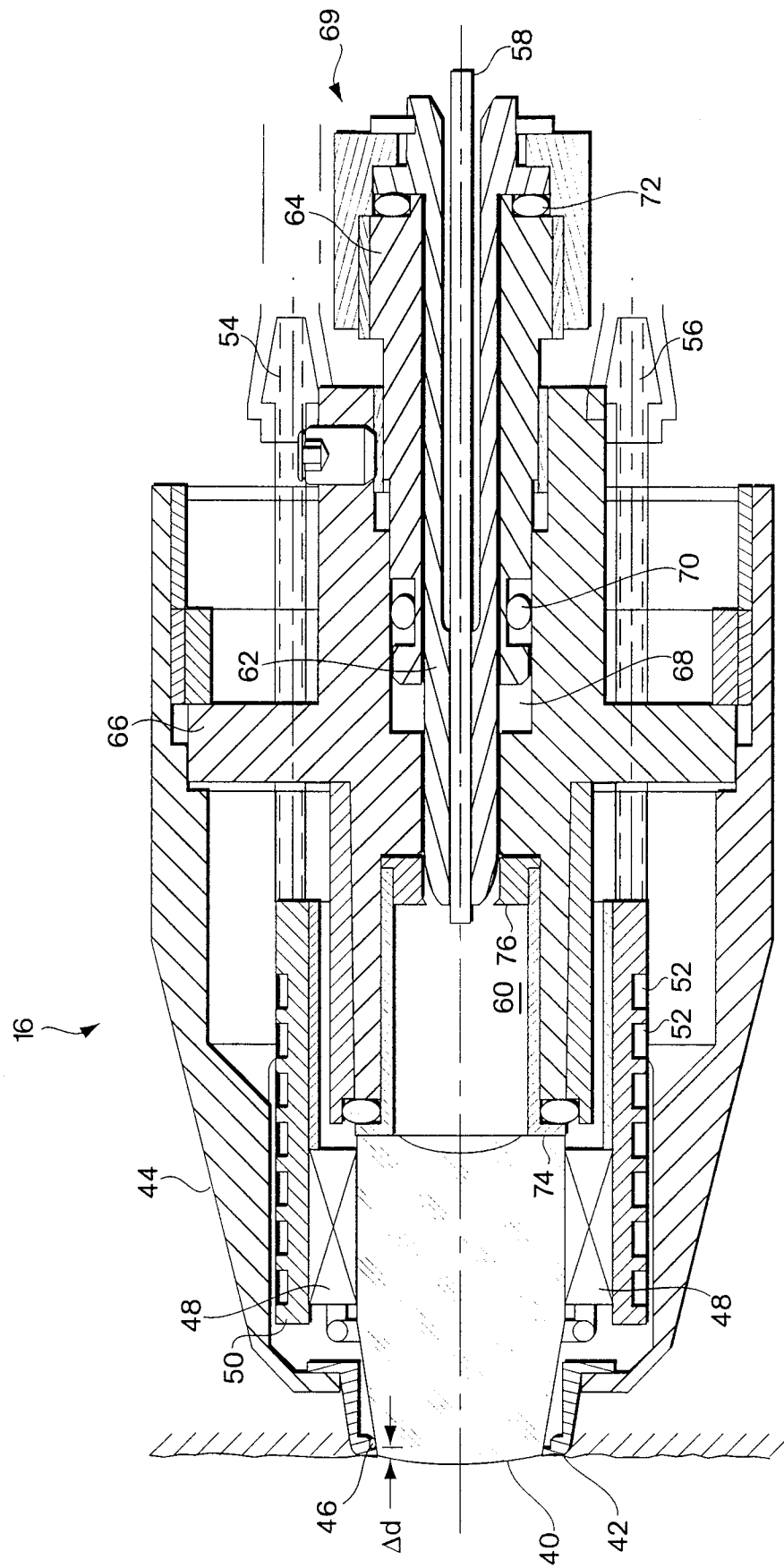


Fig. 1

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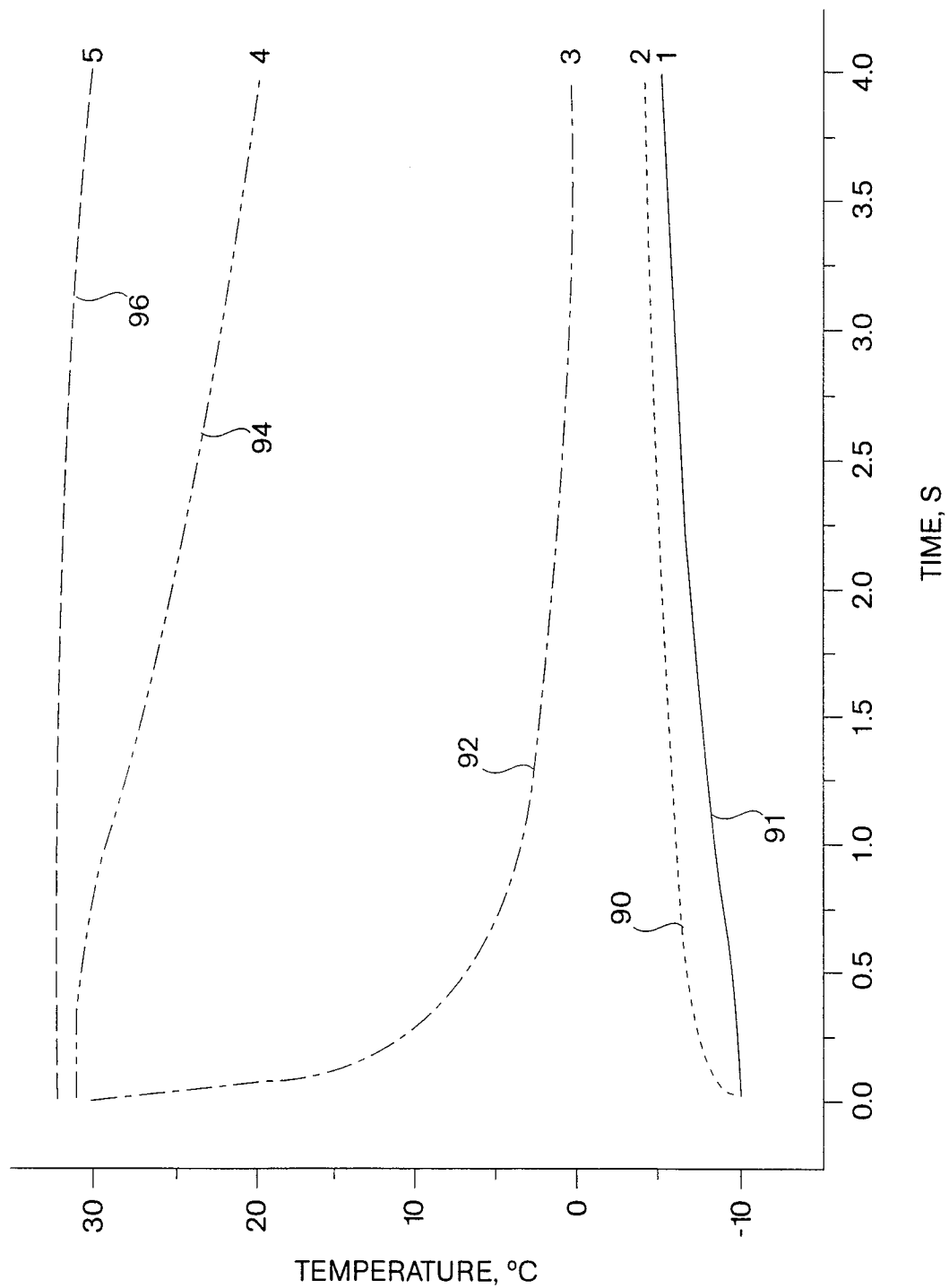


Fig. 3a

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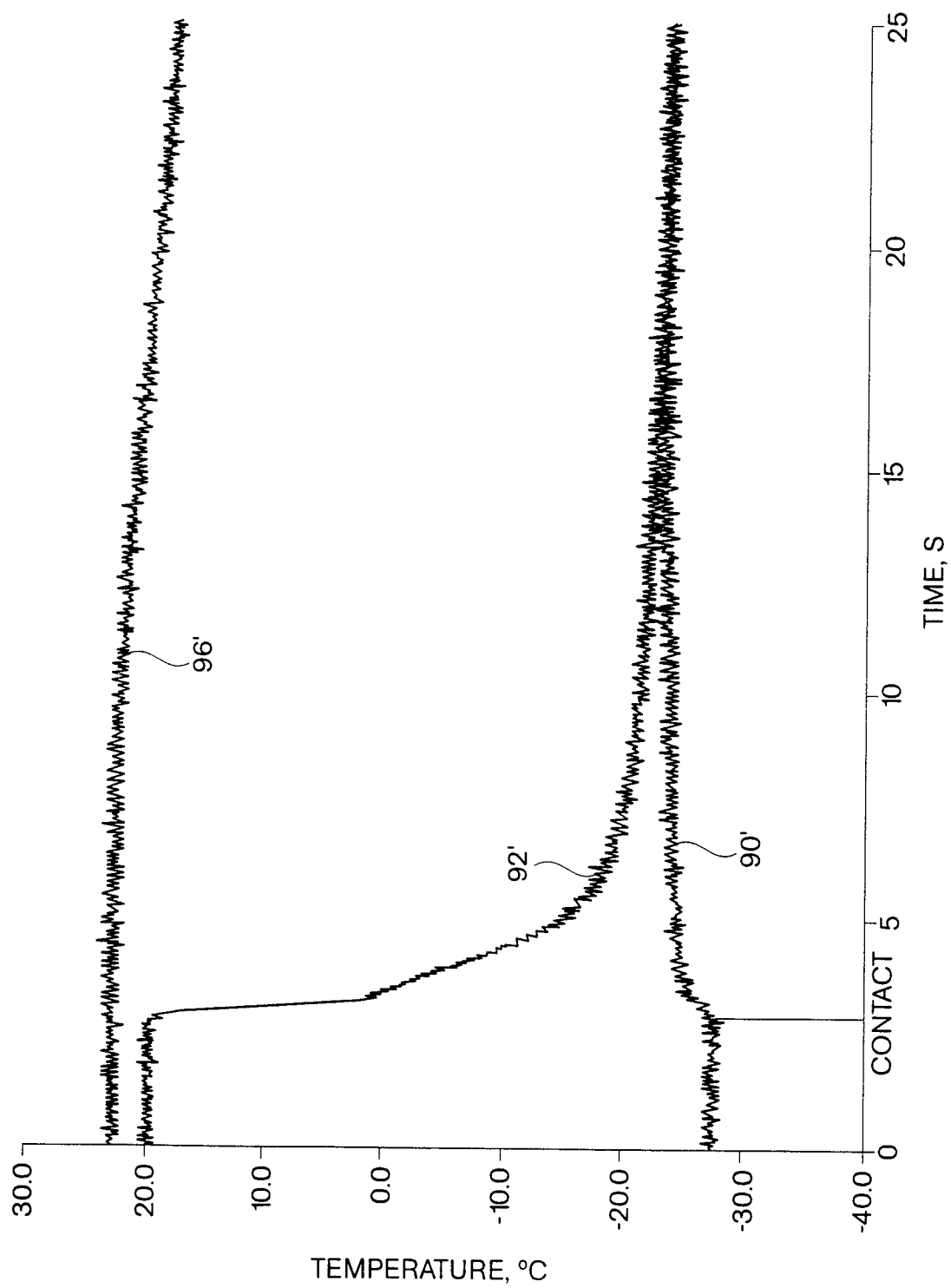


Fig. 3b

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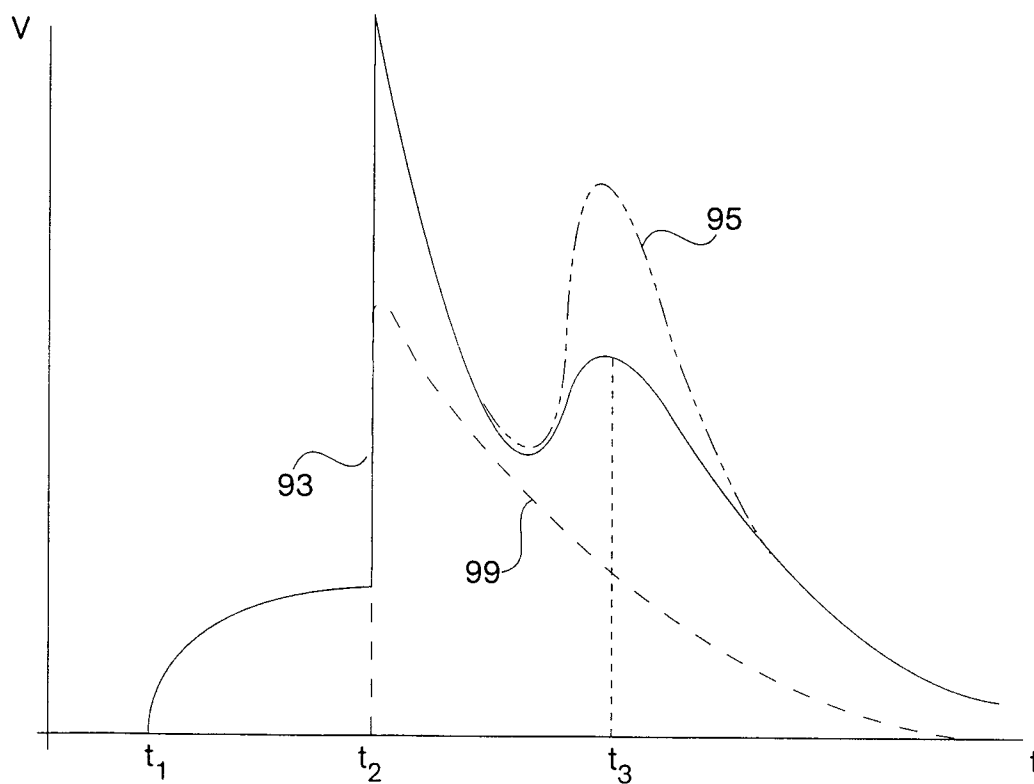


Fig. 4

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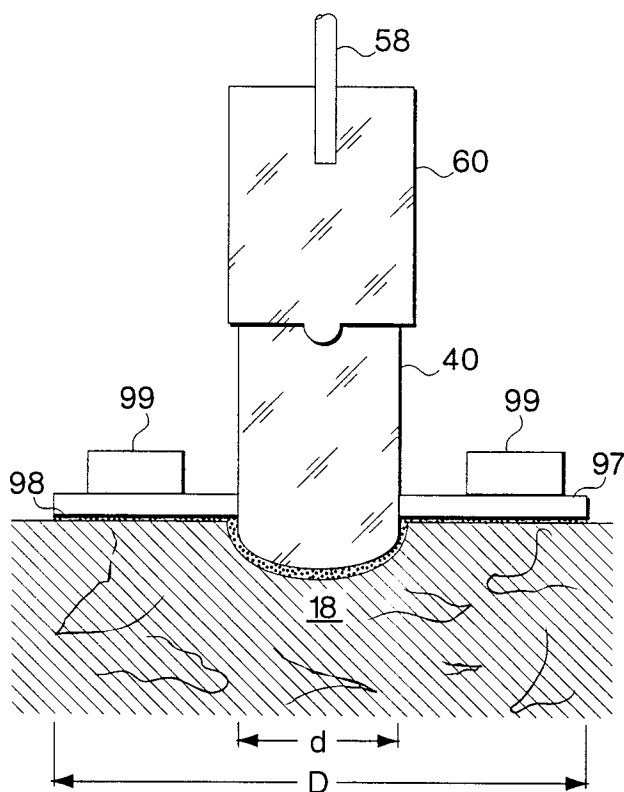


Fig. 5a

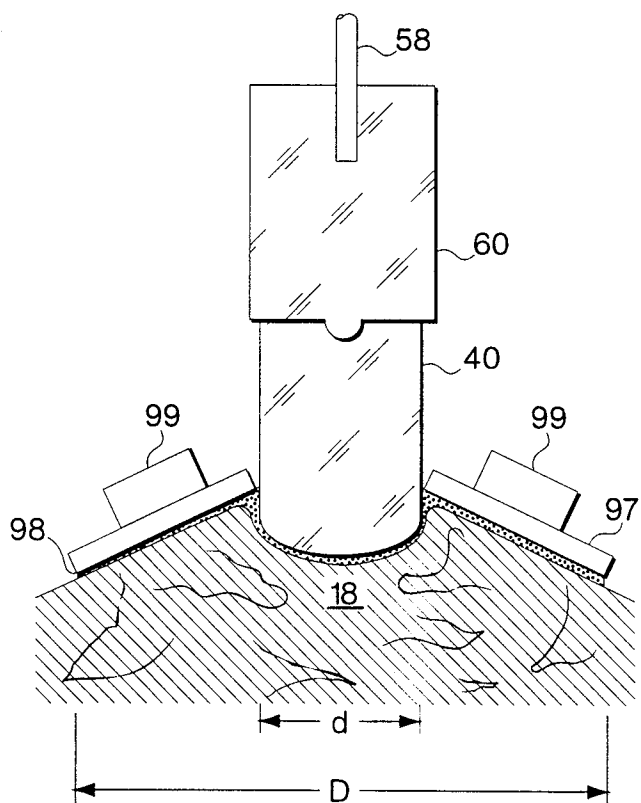


Fig. 5b

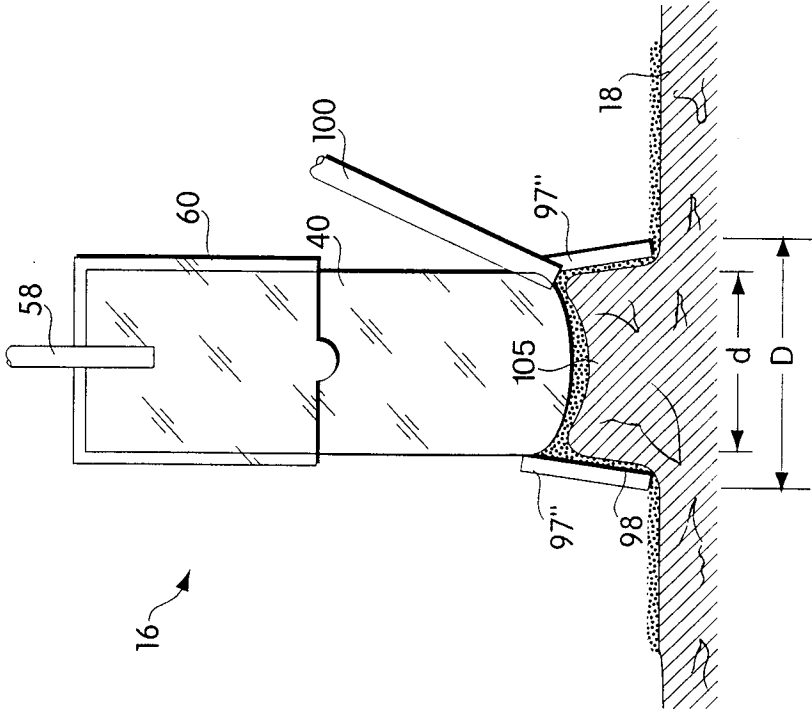


Fig. 6b

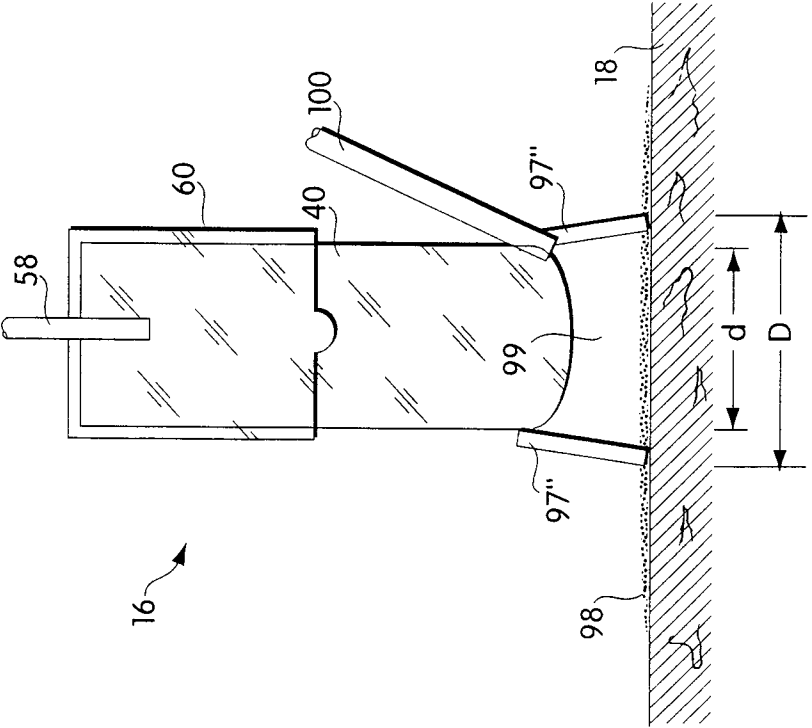


Fig. 6a

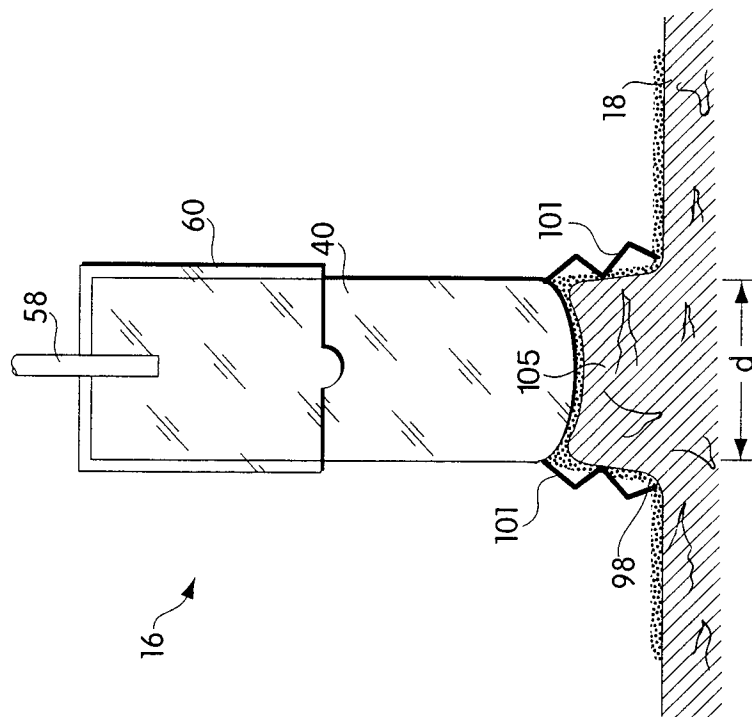


Fig. 7a

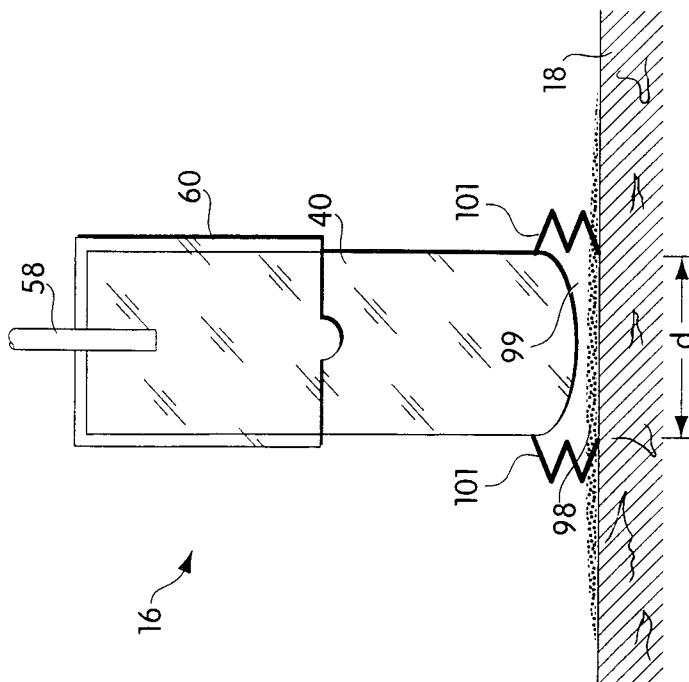


Fig. 7b

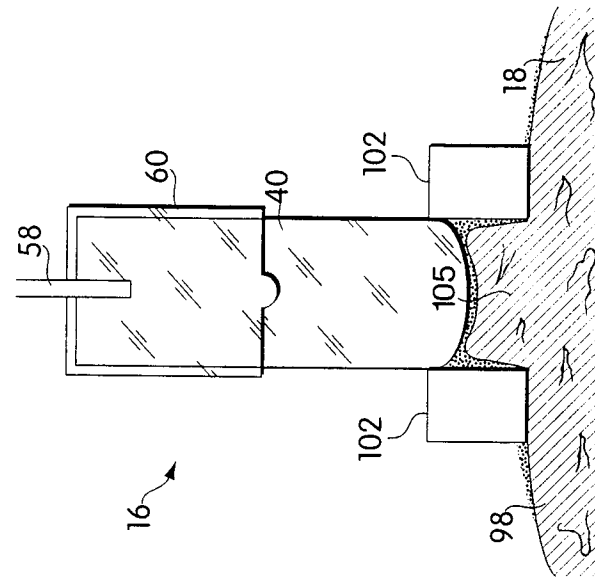


Fig. 8c

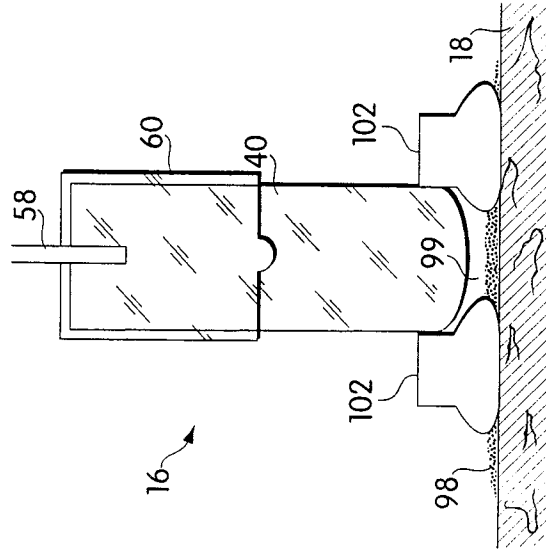


Fig. 8b

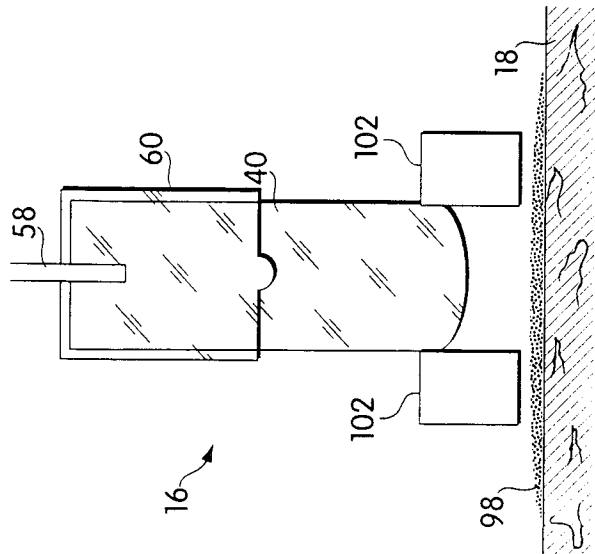


Fig. 8a

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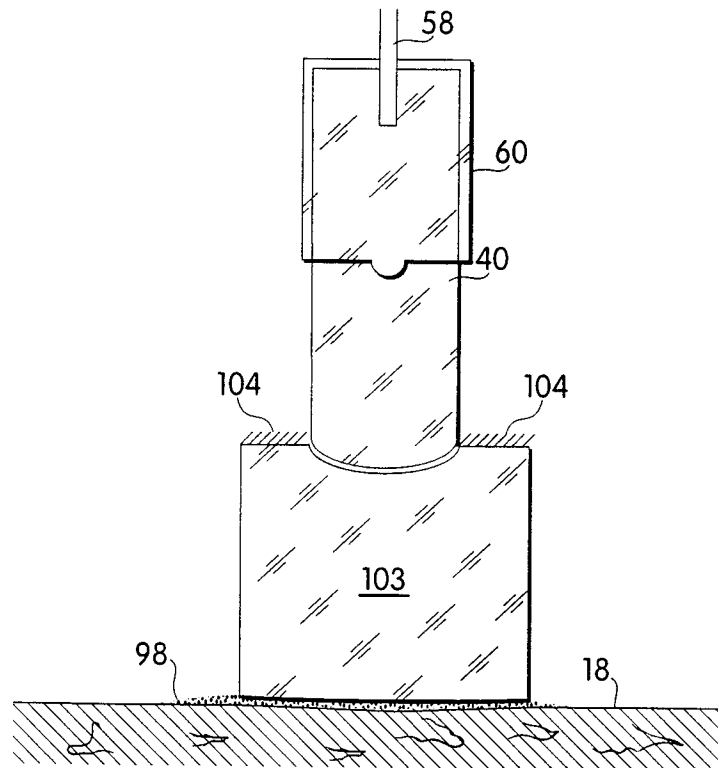


Fig. 9

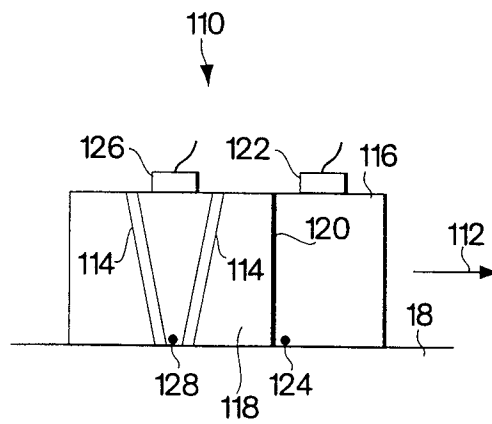


Fig. 10

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/05501

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 A61N5/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 783 904 A (ESC MEDICAL SYSTEMS LTD) 16 July 1997 see column 1, line 34 - line 40 see column 5, line 50 - column 6, line 10; figure 2 see column 6, line 32 - line 39 see column 7, line 15 - line 41	1-7, 16-18, 20,21, 55-58
Y	---	8,9,13, 14
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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"&" document member of the same patent family

Date of the actual completion of the international search

2 July 1999

Date of mailing of the international search report

09/07/1999

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/05501

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 90 00420 A (ALLARDICE JAMES TODD ;ROWLAND ADRIAN CHARLES (GB)) 25 January 1990 see page 12, line 1 - page 14, line 18; figures 1-5	38-41
Y		8,9,13, 14
A		27-37, 49,53
X	WO 97 13458 A (GEN HOSPITAL CORP) 17 April 1997 see page 7, line 22 - page 9, line 7	38-41
A		8,9,13, 14, 27-37, 49,53
X	AT 400 305 B (DIVIDA GMBH) 27 December 1995 see page 3, line 48 - page 4, line 2; claim 1	42,44,47
A	FR 2 591 902 A (COLLIN YVON) 26 June 1987 see page 5, line 10 - page 6, line 12	42-45,47
A	WO 95 32441 A (US HEALTH) 30 November 1995 see page 7, line 7 - page 10, line 10; figures 1A,1B	49-54
A	WO 98 04317 A (LIGHT SCIENCES LIMITED PARTNER) 5 February 1998 see page 7, line 29 - line 35	58,59

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/ 05501

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
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Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

SEE ADDITIONAL SHEET

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☒ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
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Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/ US 99 /05501

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1,8-15,27-41 Improving a light conductor in such a way that back-scattered radiation from the skin is reflected.
2. Claims: 16-26 Triggering onset of radiation by measuring the thermal profile.
3. Claims: 42-48 Improving physical contact with the skin by suction.
4. Claims: 49-54 A second optical waveguide applied to the first waveguide.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/05501

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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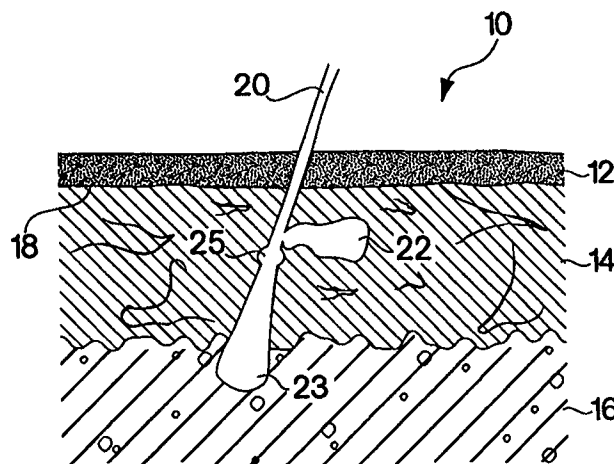
INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : A61N 5/06	A1	(11) International Publication Number: WO 99/49937 (43) International Publication Date: 7 October 1999 (07.10.99)
(21) International Application Number: PCT/US99/06475 (22) International Filing Date: 26 March 1999 (26.03.99) (30) Priority Data: 60/079,710 27 March 1998 (27.03.98) US (71) Applicants: THE GENERAL HOSPITAL CORPORATION [US/US]; 55 Fruit Street, Boston, MA 02114 (US). PALOMAR MEDICAL TECHNOLOGIES, INC. [US/US]; 45 Hartwell Avenue, Lexington, MA 02173 (US). (72) Inventors: ANDERSON, R., Rox; 399 Marrett Road, Lexington, MA 02173 (US). ALTSHULER, Gregory, B.; 8R Fernbanks Road, Wilmington, MA 01887 (US). MANSTEIN, Dieter; Apartment #513, 145 Pinckney Street, Boston, MA 02114 (US). (74) Agent: KRANSDORF, Ronald, J.; Wolf, Greenfield & Sacks, P.C., 600 Atlantic Avenue, Boston, MA 02210 (US).		(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i>

(54) Title: METHOD AND APPARATUS FOR THE SELECTIVE TARGETING OF LIPID-RICH TISSUES

(57) Abstract

A method, and apparatus are provided for targeting lipid rich tissue to effect a desired method/apparatus involving irradiating the lipid rich tissue (16) with energy at a wavelength preferentially absorbed by lipid cells, such wavelength being preferably in a band between 880 nm to 935 nm, 1150 nm to 1230 nm, 1690 nm to 1780 nm, or 2250 nm to 2450 nm with a fluency, and duration sufficient to achieve a desired treatment. For preferred embodiments the irradiation wavelength is between 900 nm to 930 nm, 1190 nm to 1220 nm, 1700 nm to 1730 nm, or 2280 nm to 2350 nm. The method, and apparatus may for example be used to target one or more sebaceous glands (22) for the treatment of acne or hair removal to target subcutaneous fat for removal thereof, or for targeting fat on an anatomical elements for various purposes.



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**METHOD AND APPARATUS FOR THE SELECTIVE TARGETING
OF LIPID-RICH TISSUES**

Related Applications

This application claims priority from provisional specification 60/079710 filed
5 March 27, 1998, the subject matter of which is incorporated herein by reference.

Field of the Invention

This invention relates to methods and apparatus for the selective heating of lipid-rich
tissue including sebaceous glands, subcutaneous fat, lipid in membranes of cells, and fat
10 surrounding organs, vessels, hair bulbs, and other anatomical elements, and/or to the selective
destruction or removal of such tissue and/or structures adjacent thereto; and more particularly
to methods and apparatus for using optical radiation in selected wavebands, which radiation
may be obtained from a laser or other suitable light source, to effect such heating, removal
and/or destruction.

15

Background of the Invention

Adipose or lipid-rich tissue, which is also sometimes referred to as "fat" or "fatty tissue",
is a common cosmetic and surgical problem, and excessive body fat may also pose certain other
health risks. Many factors, including heredity, glandular function, nutrition and lifestyle affect
20 both the extent and location of body fat. Despite dieting and exercise, many people cannot lose
fat, particularly in certain areas. Heretofore, liposuction, a procedure in which fat is removed
by a suction cannula under local anesthesia, or other forms of fat excision have been used. Fat
also occurs in pads on the face and neck and small area local liposuction has sometimes been
performed in these areas. However, liposuction is an invasive surgical procedure and presents
25 all of the disadvantages and risks to the patient involved in such a procedure, including scars
at the sites of entry into skin. Another problem with liposuction is that it is not selective in only
removing unwanted fat, but also rips out tissue in the path of the liposuction hose, including the
collagen supporting structure holding the patient's skin in place. This can result in cosmetically
unattractive sagging skin in the treated area, in addition to significant pain to the patient both
30 during and after the procedure, risk of infection and other potential problems. The trauma
caused by extreme liposuction has in some cases even resulted in the death of the patient.
Further, while liposuction can be used for the removal of deep fat, it is significantly less

effective for removing fat at a superficial level of subcutaneous fat just below the dermis. Such removal is desirable in some cases because it is less traumatic to the patient. However, it is difficult to do with a liposuction cannula without scratching the dermis, damage to the dermis not healing readily, and attempts to perform surface liposuction also result in an uneven removal
5 of fat which leaves an esthetically unattractive patterning on the patient's skin. Therefore, while liposuction is still used extensively for the removal of excess fat, it is not a desirable procedure.

Fat is also a problem in various surgical procedures where it may be difficult to locate vessels, organs or other anatomical elements on which surgery is to be performed when these elements are covered in fat, and it may be difficult to close surgical openings in such elements.
10 Performing surgery on vessels, organs or other elements covered by fat is therefore risky and current procedures for removing such fat to facilitate surgical procedures have significant limitations. Of particular concern is mesenteric fat which is a common hindrance in laparoscopic surgery. With the current trend of making surgical procedures less invasive by inserting tools through a small surgical opening, the removal of fat in the region where a
15 surgical procedure is being performed, utilizing a tool consistent with such surgical procedures, so as to facilitate remote viewing of the anatomical element being treated/operated on is therefore becoming increasingly important.

In addition, a major problem for teenagers and others is acne which originates at least in part from obstruction of outflow from a sebaceous gland. Certain drug treatments for acne
20 operate through a mechanism of decreasing sebaceous gland output. Destruction, removal, or unblocking of the sebaceous gland, which gland contains lipid-rich tissue, in a non-invasive manner are therefore desirable alternatives for treatment or prevention of acne.

Another related problem is the removal of unwanted hair, and in particular the long-term or permanent removal of such hair by the damage or destruction of the hair follicle. Many
25 techniques have been employed over the years for this treatment, including electrolysis, waxing and treatments with various forms of radiation, including light. However, electrolysis is slow and both electrolysis and waxing are painful to the patient and seldom permanent. Various radiation treatments, particularly those involving light, work more effectively for patients having darker hair than for patients with light hair and various proposals have been made over
30 the years to add a chromophore in some way to the follicle to facilitate such treatments. The use of such artificial chromophores has not heretofore been particularly successful.

Other related problems involve either removing fat, for example in the stratum corneum, under certain conditions, for example when a pressure injection is to be given, selectively porating cells having lipid-rich walls to permit substances, for example therapeutic agents, to enter the cells or to permit the removal of wanted or unwanted substances therefrom or to
5 otherwise heat or destroy lipid-rich tissue for various therapeutic purposes.

While lasers or other light sources have been proposed in the past for heating, removal, destruction (for example killing), photocoagulation, eradication or otherwise treating (hereinafter collectively referred to as "treating" or "treatment") of lipid-rich tissue such as subcutaneous fat, the lasers proposed for such procedures have operated at a wavelength where
10 lipid-rich tissue has an absorption coefficient which is generally significantly less than that for water. This presents several problems. First, lipid-rich tissue is radiation heated as a result of absorption in the tissue of radiation energy. Therefore, for wavelengths at which lipid-rich tissue does not absorb the radiation strongly, large amounts of energy must be applied to the tissue in order to obtain the requisite heating. However, in addition to significantly increasing
15 the cost of the procedure, the need for high energy poses a danger of damage to surrounding tissue or the tissue through which the radiation passes, particularly since most such tissue is primarily composed of water which absorbs the radiant energy much more at these wavelengths.

This is a particular problem for subcutaneous fat which generally starts at a depth of at least 1 to 4 mm into a patient's skin, and may be deeper for some individuals or some body
20 areas. Therefore, in order for the radiation to target to the subcutaneous fat to cause selective heating or destruction thereof, it must pass through several millimeters of tissue formed primarily of water. Since water preferentially absorbs at these wavelengths, most of the incident radiation is absorbed in the skin prior to reaching the subcutaneous fat and, since skin is a scattering medium, incident light is also scattered and reflected from the patient's skin, resulting
25 in a very small fraction of the incident light reaching the subcutaneous fat. Therefore, due to both the small fraction of the applied energy reaching the subcutaneous fat and the low absorption of this energy by the fat, in order to get enough energy to the subcutaneous fat at these wavelengths to be effective, large amounts of radiation would need to be applied to the overlying epidermis and dermis. Since such high levels of radiation absorbed in the dermis or
30 epidermis would cause significant thermal damage to these skin layers at the prior art wavelengths, treatment/destruction of fat cannot be performed through the skin, but must be performed by providing an opening, for example a surgical opening, through the skin to provide

direct contact with the fat tissue to be treated. Even when the radiation is applied directly to the fat tissue to be treated, high energy is required and great care must be exercised to avoid excessive radiation of surrounding or underlying tissue so as to minimize damage thereto. Other prior art fat treatment techniques, involving the use of either microwaves or ultrasound, either alone or in conjunction with liposuction, to melt or loosen the fat and to remove it or have it absorbed into the body, have either proved not to be effective for fat removal, have posed potential health hazards to patients, either actual or perceived, or have still involved invasive procedures, the risk of which have been discussed earlier.

A need therefore exists for an improved technique for heating and destroying, or otherwise targeting lipid-rich tissue, including, but not limited to, subcutaneous fat, sebaceous gland, lipid in membrane cells and fat covering anatomical elements on which surgical or other procedures are to be performed, which does not suffer the limitations of prior art techniques, including liposuction, and which is significantly more selective than the prior art in the destruction of lipid-rich tissue over tissue containing water so as to safely achieve the desired effects on lipid-rich tissue in performing a therapeutic procedure.

Summary of the Inventions

In accordance with the above, this invention provides a method and apparatus for selectively targeting lipid-rich tissue to effect a desired treatment, the method/apparatus involving irradiating the lipid-rich tissue at an infrared wavelength at which the ratio of absorption of the radiation by lipid-rich tissue to absorption by water is 0.5 or greater, and preferably greater than one. In particular the irradiation is preferably at a wavelength between 880-935 nm, 1150 to 1230 nm, 1690 to 1780 nm, or 2250 to 2450 nm with a fluence and for a duration sufficient to treat such lipid-rich tissue. For preferred embodiments, depending on application, the irradiation wavelength is between approximately, 900 to 930 nm, 1190 to 1220 nm, 1700 to 1730 nm, or 2280 to 2360 nm, with approximately 920 nm, 1210 nm, 1715 nm, and 2300 nm being most preferred wavelengths. While the fluence and duration of irradiation will vary somewhat with the patient undergoing treatment, the anatomical location of the tissues being treated, the radiation source and wavelength, the size of the lipid-rich tissue being treated and other factors, for preferred embodiments the treatment fluence may for example be approximately 0.5 J/cm² to 500 J/cm², with the duration of treatment pulses being

approximately 10 μ s to several seconds, or even minutes for photothermal effect, and less than 1 μ s (i.e., generally 1 μ s to 1 ns) for photomechanical effects.

Where the lipid-rich tissue being treated is one or more sebaceous glands, irradiating the tissue/gland is performed by applying the energy at an indicated wavelength, which wavelength is preferably in one of the higher bands, to the skin surface overlying such one or more sebaceous glands. Where the lipid-rich tissue is subcutaneous fat, energy may be applied to the skin surface overlying the subcutaneous fat to be treated. Where either the sebaceous gland or subcutaneous fat is treated through the overlying skin, and particularly for subcutaneous fat, the radiation is preferably applied through an applicator which applies pressure to the skin above the lipid-rich tissue being treated. This pressure reduces the distance from the radiation-applying applicator to the lipid-rich tissue being targeted, removes blood from the area above the fat tissue being targeted and compresses such overlying tissue to reduce scattering and enhance optical focusing of radiation on the treatment area. It is also desirable that the skin above the area being treated be cooled to a selected depth, which depth is above that of the lipid-rich/fat tissue being targeted. Thus, cooling could be deeper for the treatment of subcutaneous fat, where the cooling could be most of the way through the dermis, while the cooling would be to a much shallower depth, perhaps only to the dermis/epidermis (DE) junction, where the sebaceous gland is being treated. While radiation in the higher bands can be used, and may be preferable because of the higher absorption coefficient of fat in these bands, for treating the sebaceous gland which is relatively close to the skin surface, absorption by water at these wavelengths make it difficult to reach subcutaneous fat, and radiation in the lower bands, for example in 1150 to 1230 nm range where water is less absorbent may therefore be preferable for treating subcutaneous fat. In addition to or instead of pressure being applied to the skin, a fold of skin may be drawn into a recess in a radiation delivery head in a suitable manner and radiation applied to the recess from at least two directions. This has a number of beneficial effects, including reducing the distance from the radiation source to the lipid tissue, increasing the radiation at the desired depth without increasing radiation in regions above the target area and, where a retroreflection technique to be discussed later is utilized, substantially eliminating radiation loss as a result of the scattered radiation reflected from the patient's skin. Alternatively, to increase the local intensity for treatment of subcutaneous fat when delivered through the overlying skin, a convergent incident beam is advantageous to compensate for losses due to optical scattering and absorption in the dermis.

While the sebaceous gland may be heated to destroy the gland as part of an acne treatment, the sebaceous gland may also be heated to cause destruction of adjacent areas of a hair follicle, for example the stem cells of the hair follicle as a treatment to achieve hair removal and impede regrowth. Radiation in the indicated wavelengths may also be applied selectively to cells having lipid-rich membranes to porate the membranes to for example permit selective drug delivery to the cells or for other purposes for lipid-rich cells or tissue may be otherwise targeted and heated for affecting some other therapeutic function. Since the radiation fluence, pulse duration, wavelength and other factors may be carefully controlled, and the area to which the radiation is directed may also be controlled, selective lipid-rich cells may be non-invasively targeted to achieve the above and other therapeutic affects.

Where subcutaneous fat is being non-invasively treated, duration of radiation pulse and the temperature to which the fat or lipid tissue is heated are critical to the desired results. For example, at increased temperature, fat is altered by a biochemical reaction or lipolysis, while for higher temperatures and sufficient pulse duration, fat cells are killed, permitting the cells and liquid lipid therein to be absorbed. At still higher temperatures, cell membranes are destroyed, permitting lipid pools to be formed. These pools may also be absorbed but, since free fatty acid in lipid can be toxic in sufficient quantity, if substantial quantities of fat cell membranes have been destroyed, permitting a large lipid pool to be formed, it is preferable to remove the lipid, for example with a cannula or needle. The heated collagen of supporting structure may react to provide a more pleasing skin appearance after treatment and avoid sagging folds of skin or skin depressions where the lipid tissue has been destroyed. While all of the fat in a subcutaneous layer may be treated, it is difficult to get sufficient energy deep into the fat, so treatment is generally restricted to a surface layer of the fat. Repetitive treatments may be performed to remove successive layers of the subcutaneous fat.

While non-invasive procedures are preferable, subcutaneous fat may also be treated by passing a probe through the skin to the subcutaneous fat to be treated. The probe, which may for example be a needle, may be passed into the subcutaneous fat at an angle to the skin surface and the probe may be moved both in and out of the skin and rotated about its skin entry point to irradiate and treat subcutaneous fat over a selected area. This needle or probe may also contain a cannula for removing liquid lipid pooled as indicated above from the radiation treatment

Where lipid-rich tissue/fat surrounds a vessel, organ or other anatomical element on which a surgical or other procedure is to be performed, the irradiation may be performed by use

of a tool which is in at least near contact, and preferably in contact, with the fat to be treated, the element treating the fat to expose the anatomical element on which the procedure is to be performed. Because radiation for this embodiment does not need to pass through water rich tissue to reach the fat, wavelengths in the higher bands would normally be used for this
5 procedure.

While various light sources might be utilized to obtain optical energy within the required bands, and in particular at the preferred wavelengths, including a suitably filtered tungsten lamp, an optical parametric oscillator, a Raman convertor or shifter, a color center laser or a tunable dye laser, the preferred light source at the desired wavelengths is a diode laser or lasers
10 with flashlamp or diode pumping which will be described in greater detail later.

The foregoing and other objects, feature and advantages of the invention will be apparent from the following more particular description of preferred embodiments of the invention as illustrated in the accompanying drawings:

15

In the Drawings

Fig. 1 is a diagrammatic sectional view of human skin illustrating both a hair follicle with a sebaceous gland and subcutaneous fat.

Fig. 2A is a sectional view illustrating an area of subcutaneous fat under treatment in accordance with the teachings of a first embodiment of this invention.

20 Fig. 2B is a sectional view illustrating an area of skin, either subcutaneous fat, sebaceous gland or other targeted lipid-rich tissue, under treatment in accordance with an alternative embodiment of the invention.

Fig. 3 is a sectional view illustrating a section of skin with subcutaneous fat under treatment employing another alternative embodiment of the invention.

25 Fig. 4 is a sectional view illustrating a tool being utilized to clear fat from a vessel on which a surgical procedure is to be performed in accordance with the teachings of this invention.

Fig. 5 is a graph illustrating the coefficient of absorption of water and of human fatty tissue as a function of wavelength.

30 Fig. 6 is a graph illustrating the ratio of human fatty tissue coefficient of absorption to water coefficient of absorption as a function of wavelength.

Detailed Description

Fig. 1 is a simplified sectional view through a piece of human skin 10 illustrating the major skin layers. The outermost layer is the epidermis 12 which overlies the dermis 14. Under the dermis is a layer of subcutaneous fat 16. The epidermis is typically relatively thin, on the order of 0.1 mm, although this thickness varies for different parts of the body, with the lower portions of the epidermis near the DE junction 18 containing quantities of melanin which vary with the pigmentation of the individuals skin. The thickness of dermis layer 14 varies from approximately 1 to 5 mm depending on the part of the body and on the individual, and may be thicker in some instances. The lower third of the dermis typically contains numerous lobules of fat. Subcutaneous fat 16, which may be several centimeters thick, therefore generally starts at a depth of a little less than 1 mm to approximately 4 mm from the skin surface.

Fig. 1 also illustrates a single hair follicle 20 with an adjacent sebaceous gland 22. Hair follicle 20 has a bulb or papilla 23 and stem cells in a bulge region 25, both of which are involved in the growth and regrowth of hair from the follicle. Sebaceous glands 22 are formed primarily of fat/lipid-rich tissue. The cells lining the outer portion of sebaceous glands are called sebocytes. These cells migrate inward, synthesizing a lipid-rich fluid called sebum as they differentiate and finally are shed. The sebum flows outward through a duct into the infundibulum ("pore") of the follicle. The greasy, oily material which accumulates on the surface of skin is sebum, after flowing out of numerous follicles. When the outflow from a sebaceous gland becomes clogged, it may result in the formation of an acne pimple. This is a particular problem for larger sebaceous glands, for example those on the face and upper back, which are the most common sites of acne. Sebaceous glands are typically found approximately 1 mm below the skin surface, although they may be at greater depths in some instances, and are in the dermal layer 14 as shown in Fig. 1.

While as was discussed earlier, various techniques have been used in the past to remove unwanted fat, and there has been limited use of lasers for treating fat tissue, since there was not selective absorption by lipid-rich tissue for the wavelengths at which such procedures were conducted, such fat treatment could generally be done only through a surgical procedure which permitted the laser to be brought directly adjacent or in contact with the fat tissue to be treated. However, because of the low absorptions of fat at such wavelengths, and the high ratio of water absorption to fat absorption, very high energy was required for treatment and extreme care had to be exercised so as to avoid unintended damage to other tissue either adjacent to or underlying

the fat tissue to be treated. As a result, such procedures have not been used to any significant extent.

In order to determine a preferential wavelength for lipid absorption, it should be appreciated that the temperature rise in a given tissue as a result of absorbing a given amount
5 of energy is a function of the density of the tissue and its heat capacity. When this temperature increase for absorbed energy is compared for water and fat or lipid-rich tissue, it is found that the temperature rise in the lipid-rich tissue for a given energy absorption is 1.8 to 2 times that for water. Therefore, lipid-rich tissue need absorb 0.5 to 0.6 as much energy to achieve the same temperature rise as for water. Thus, for purposes of the following discussion, it will be
10 assumed that lipid tissue preferentially absorbs at a wavelength for which the coefficient of absorption for fat is at least 0.5 that of water, although this ratio for preferred wavelengths is at least 1 and is 1.5 or higher for selected wavelengths.

Thus, as illustrated in Figs. 5 and 6, and in accordance with the teachings of this invention, it has been discovered that for wavelengths between approximately 880 nm and 935
15 nm, 1150 and 1230 nm, 1690 and 1780 nm, or 2250 and 2450 nm, lipid has at least 0.5 the absorption of water, and generally greater absorption than water, water being the major constituent of lipid-poor tissue. This absorption is attributed to a vibrational mode in the C=H and C-H bands common in lipids. These wavelength bands also are readily compatible with silica optics. For these regions, the absolute absorption by both water and lipid increases with
20 increases in the wavelength (i.e., both water and lipid absorb most strongly in the 2250 to 2450 nm range and absorb least strongly in the 900 to 930 nm range). The ratio of lipid absorption to water absorption is also greater for the higher wavelengths, being over 1.5 for maximas at approximately 1715 nm and 2300 nm. Therefore, radiation within the above-indicated wavelength bands, and in particular radiation at or near various maxima in these bands such as
25 925 nm, 1210 to 1230 nm, 1715 nm, or 2300 nm would be particularly effective for treating lipid-rich tissue such as sebaceous glands or subcutaneous fat. However, the depth which light/radiation reaches in a patient's skin is inversely proportional to light absorption above such depth. Since water is the primary constituent of skin tissue, water absorption is a controlling factor in the depth which radiation of a particular wavelength may reach in a patient's skin.
30 Therefore, radiation in the 900 to 930 nm band and 1210 to 1230 nm band which are most weakly absorbed by water, while still being at least somewhat strongly absorbed by fat, are the currently preferred radiation bands for non-invasively treating subcutaneous fat, where the

radiation generally needs to reach at least 3 to 4 mm within the patient's skin. However, radiation in the higher bands, and particularly at 1200 nm (with focusing), 1715 nm, and 2300 nm wavelengths, may be preferable for treating the sebaceous gland which is generally located only 1 mm into the patient's skin, since fat absorbs more strongly at these wavelengths and water absorption in the overlying skin is not as big a factor. The longer wavelengths could also be used where a suitable light emitting probe is positioned adjacent the fat to be ablated, for example to clear fat from a vessel, organ or the like or where a needle is used to get to subcutaneous fat.

The first issue in implementing the teachings of this invention is to find a radiation source adapted for generating sufficient radiation at the required wavelengths. Unfortunately, while commercially available lasers or other radiation sources are available for the 900-930 nm range and YAG lasers operate at approximately 1060 and 1300 nm, current commercially available lasers/radiation sources are not normally adapted for generating radiation at the other preferred wavelengths. However, there are lasers and other radiation sources suitable for generating such radiation.

For example, the following light sources with wavelengths around 920, 1200, 1715, or 2300 nm can be used for fatty tissue targeting:

1. Tungsten lamp or an arc lamp with an absorptive or reflective filter which filters the required spectral region. Optimum lamp temperature is in the region 1300-2000 K.
2. Tungsten lamp or an arc lamp with a luminescence filter with a peak of luminescence at one of the spectral regions described above. As a filter, the following can be used: crystals with color centers, liquid dyes or dyes in a solid matrix.
3. Diode lasers, such as GaAs (920 nm), AlGaSbAs (1200, 1215 nm), InGaAsP/InP (1715 nm), InGaAs (2300 nm).
4. Lasers based on crystals with color centers and lamp or laser pumping. These would include crystals NaF with F^{2+} centers (1200 nm) or KCl with F^{2+} centers (1215 nm) or KClLi with F^{2+} centers (2300 nm).
5. Lasers with non-linear wavelength conversion; optical parametric oscillators (OPO) or Raman converters can be used as such non-linear converters. Solid state lasers can be used for pumping (Nd laser, Ho laser, Er laser, fiber laser etc.) of OPO or Raman converter.

6. One of the most effective lasers can be a lamp pumped solid state laser with correct spectral lines. For example crystals with ions Er^{3+} can generate in the region 1200 nm ($^4\text{S}_{3/2} \rightarrow ^4\text{I}_{11/12}$) and 1715 ($^4\text{S}_{3/2} \rightarrow ^4\text{I}_{9/2}$).

For operating in the 1700 to 1730 nm range, one suitable laser is a potassium cadmium laser with the matrix $\text{KCd}(\text{WO}_4)_2$ which is doped with Er^{3+} (erbium) ions. The concentration of Er^{3+} ions should be in the range of 1-10 percent, with the optimal concentration being approximately 2-5 percent. The energy level transition $^4\text{S}_{3/2} \rightarrow ^4\text{I}_{9/2}$ should be used for laser generation. For both levels $^4\text{S}_{3/2}$ and $^4\text{I}_{9/2}$, Stark broadening and the wavelength for maximum laser output depend on the relative orientation of the crystal axis, laser radiation axis and polarization of laser radiation. When the orientation is such that the axis of the laser beam is at an angle greater than 45 degrees with the crystal line axis [010], the spectral maximum of the laser output is at the desired 1715 nm wavelength. Maximum efficiency is achieved when the axis of the laser beam lies in the plane determined by the crystalline axis [100] and [001] and is directed along the optical axis N_m which forms an angle of 24 degrees with crystalline axis [100]. If the same crystal is used for laser generation along the crystalline axis [010], the wavelength of laser generation for the same transition is 1730 nm. Flashlamps, laser diodes, other lasers or other pump mechanisms can be used to pump the above crystal in order to achieve the desired wavelength output.

In order to obtain maximum efficiency, the following scheme might be used to provide the desired radiation:

A diode laser generating an output at approximately 920 nm is used to pump a Yb doped glass or fiber with a laser wavelength of 1100 nm. This output is then frequency-doubled to obtain a wavelength of 550 nm which is the most efficient pumping wavelength and may be utilized for direct pumping of the $^4\text{S}_{3/2}$ level. The maximum efficiency would be 0.6 (diode) x 0.3 (fiber laser) x 0.7 (doubling) x 0.3 (Er laser) = 3.75 percent. With this laser, it is possible to achieve generation of wavelengths 850 nm ($^4\text{S}_{3/2} \rightarrow ^4\text{I}_{13/2}$ transition) and 1220 nm ($^4\text{S}_{3/2} \rightarrow ^4\text{I}_{11/2}$ transition), along with the generation at wavelengths 1715 nm or 1732 nm. The laser can work simultaneously at various combinations of these wavelengths including:

$\lambda = 1715 \text{ nm}$ and $\lambda = 850 \text{ nm}$, or
 $\lambda = 1715 \text{ nm}$ ($\lambda = 1730 \text{ nm}$) and $\lambda = 1210 \text{ nm}$, or
 $\lambda = 1715 \text{ nm}$ ($\lambda = 1730 \text{ nm}$), $\lambda = 1210 \text{ nm}$ and $\lambda = 850 \text{ nm}$.

Laser light from pumping diode laser (920 nm) can also be used for selectively heating fat. Control over the spectral distribution is achieved by changing mirrors or by a dispersive element inside the laser cavity.

Radiation at 1730 nm, may be obtained if lasers based on YLF, YAG, YAL, YSGG or
5 a fiber doped with Er^{3+} ions are used. In these lasers, the same transition where $^4\text{S}_{3/2} \rightarrow ^4\text{I}_{9/2}$ is used, and the ion concentrations and the pumping methods would be substantially the same as for the preferred laser indicated above, but as indicated previously, would result in an output at 1730 nm, which is not one of the most optimal wavelengths for lipid-rich tissue ablation, although still suitable for this purpose. Its combination with $\lambda = 1210$ nm and $\lambda = 850$ nm is
10 also possible. Pumping methods and concentration of active ions is the same as for the $\text{KCd}(\text{WO}_4)_2:\text{Er}^{3+}$. The concentration of Er^{3+} ions should be in the range 1-50%, with an optimal ion concentration being in the range 2-5%.

Radiation at 1730 nm may be achieved using for example, an $\text{YLF}:\text{Er}^{3+}$ with concentration of Er^{3+} 25% laser with flashlamp pumping. For this laser, the maximum output
15 energy is 1 J, slope efficiency is 0.5 %, repetition rate is 4 Hz and the pulse width is 0.4 ms.

Certain diode lasers may also be utilized to generate radiation within the desired wavelength ranges. For example, a laser based on $\text{InGaAsP}/\text{InP}$ can generate laser output in a range of wavelengths about 1700 nm with fine temperature tunability and stabilization. Blackbody sources, such as a tungsten lamp with suitable optical filters, can also be used to
20 produce the desired radiation. However, the spectral power and tissue selectivity of such light sources would be less than for laser sources. The optimal temperature of the heat source should be about 1700 degrees K, with approximately 5 percent of the radiation of the lamp operating at this temperature being in the spectral region between 1700 nm and 1760 nm. Further, while the desired wavelengths can also be achieved by a tunable laser like a dye laser, free electron
25 laser, color center laser or Raman shifter, the efficiencies of these lasers is low and they are very expensive. They are therefore not as practical as other sources for this application. Finally, an optical parametric oscillator (OPO) with pumping from a solid state laser or a fiber laser could also generate energy at the desired wavelengths. An OPO has maximum efficiency only for very short pulses, and would be most useful therefore when treatment is accomplished by
30 photomechanical or photodissociation at 1 ns to 4 fs interactions. Other light sources generating radiation within the indicated wavelength band might also be utilized in appropriate applications.

The time of exposure at a given site can be effectively used over a very wide range, but is preferably within either of two regions causing photothermal or photomechanical effects. For photothermal damage, or necrosis of lipid-rich tissues including fat and sebaceous glands, exposure durations of 0.1 ms to several minutes and sometimes higher are desirable, depending
5 on the size of the targeted structure (for example the sebaceous gland diameter or subcutaneous fat depth being treated). For photomechanically-mediated damage, or necrosis, e.g. by violent castation, shock waves, or spallation, an exposure of less than 1 microsecond is desirable, and less than 10 μ s is most preferred. The longer exposure duration can be generated for example by a flashlamp-pumped laser, scanned or shuttered CW laser, or conventional sources described
10 above. The shorter exposure durations, less than 10 μ s can be generated by Q-switching or mode-locking of laser cavities, or by an OPO or Raman-shifted Q-switched laser as described above.

Fig. 2 illustrates one way in which the teachings of this invention might be utilized to non-invasively treat either subcutaneous fat 16 (as shown in the figure), at least one sebaceous
15 gland 22 or other targeted lipid-rich tissue. For this embodiment of the invention, an applicator 30, which could for example be of the type shown in U.S. Patents 5,595,568 or 5,735,844, is utilized. Applicator 30 may have a lens 32 or other suitable contact element at the front end thereof, which element is adapted to be in pressure contact with the upper surface of epidermis 12, thereby deforming the skin in the contact area for example as shown in Fig. 2. Applying
20 pressure to the skin in this way provides a number of advantages. First, the pressure reduces the distance between the laser source and the sebaceous gland 22/ subcutaneous fat 16, thereby reducing the amount of tissue through which the light must pass prior to reaching the area under treatment. While radiation within the indicated bands is preferentially absorbed by the lipid-rich tissue, there is still absorption by the water/blood-containing tissue above the lipid-rich
25 tissue being treated. Therefore, the greater the reduction in the quantity and thickness of this tissue, by for example tension, the less energy is lost in this tissue, resulting both in more energy being available for treatment at the desired location and in less heating, and therefore less potential thermal damage, to the lipid-poor tissue not under treatment.

The second advantage is that if the pressure is above the body's blood pressure (e.g.,
30 about 3 psi), the pressure will force blood out from under the applicator, further reducing absorption in the lipid-poor tissue through which the radiation passes. It has also been found that compressed tissue causes significantly less scattering of light energy passing therethrough,

or in other words is more transparent to such light energy, when under significant pressure than when not under such pressure. Not only does this phenomenon reduce radiant energy loss, and thus heating in the tissue above the tissue under treatment, but it also permits more effective focusing of light energy to facilitate heating and/or damage of only desired tissue. Thus, light
5 could be focused to a depth of approximately 1 mm for treatment of lipid-rich sebaceous glands to for example treat an acne problem or for hair removal, and could be focused to a depth of for example 3 or 5 mm for treatment of subcutaneous fat 16. Fig. 2 shows an exemplary such focused radiation beam 34 being directed to the upper portions of subcutaneous fat layer 16.

However, while applying pressure has some advantages, it is also disadvantageous in
10 that blood flowing through the dermis is one effective way of removing heat so as to protect this area. This disadvantage needs to be balanced against the previously discussed advantages in deciding on whether to utilize pressure.

One problem with applying energy to the sebaceous gland 22 or to subcutaneous fat 16 through the overlying epidermis and dermal tissue is that, even though the overlying tissue do
15 not preferentially absorb radiation at the indicated wavelengths, they do as can be seen from Fig. 5, and depending on wavelength, absorb significant radiation and can therefore become heated. Such heating can cause potential temporary skin damage or permanent scarring, with permanent scarring occurring primarily in the dermis 14. Blistering, peeling, and depigmentation are other potential adverse affects which may result from the heating of tissue
20 above the lipid-rich tissue under treatment.

Therefore, it is preferable that the epidermis and dermis above the lipid-rich tissue being treated be cooled at least prior to, and preferably both prior to and during, the application of the radiation to minimize thermal damage to tissue in these areas. However, it is also important that the cooling not extend to the lipid-rich tissue being treated since such cooling would impede
25 the treatment of this lipid-rich tissue and may prevent the desired treatment thereof. Therefore, when the sebaceous gland is being treated, cooling should not extent below or much below the DE boundary layer 18, and certainly should not extend much beyond 1 mm from the skin surface. Where subcutaneous fat 16 is being treated, the cooling may extent several millimeters into the dermis, depending on the thickness thereof. The cooling may be performed in the
30 manner indicated in the before-mentioned patents or by other techniques known in the art. In particular, cryogenic cooling may be utilized to cool the skin to a predetermined depth prior to irradiation, or contact piece 32 may be cooled by flowing water or gas, or preferably by

semiconductor Peltier effect cooling as taught in co-pending application S.N. 08/759,136. The temperature of for example contact piece 32 and the time during which this piece is in contact with the skin prior to irradiation will be primary factors in determining the depth of cooling.

The energy or fluence required to heat to a desired temperature and/or destroy targeted fat and the duration of the light pulses used for this purpose will vary, sometimes significantly, with the individual being treated, the area of the body being treated, the specific lipid-rich/fat tissue which is to be treated and the wavelength utilized. For a sebaceous gland 22 having a diameter which is generally in the 0.5 to 3 mm range, which is typical for sebaceous glands being treated which are frequently larger sebaceous glands, a fluence of approximately 10 J/cm² to 500 J/cm² applied for a duration of approximately 10 ms to one second depending on the size of the gland, should result in destructive heating or other treatment of sebaceous glands in most instances, particularly if the pressure and cooling procedures discussed in the preceding paragraphs are followed. Higher fluencies are required if shorter wavelengths are used (for example 920 nm or 1200 nm) because of the lower absorption coefficient of fat at these wavelengths.

While because of the higher absorption of lipid tissue at the longer wavelengths, wavelengths such as 1715 nm, or 2300 nm may be utilized for targeting of a sebaceous gland 22 or for treatment when the light source is adjacent the lipid-rich tissue, for non-invasive treatment of subcutaneous fat, particularly in region where the dermis is 3 to 4 mm thick, the high absorption of water at these wavelengths effectively prevents radiation at these wavelengths from penetrating to reach the subcutaneous fat layer, even when relatively high fluence signals are utilized. However, at the shorter wavelengths, for example 920 nm or 1200 nm, water is significantly less absorbent, permitting a significant percentage of the applied radiation to reach at least the upper level of subcutaneous fat layer 16. However, as may be seen from Fig. 5, fat also has a significantly lower coefficient of absorption at these wavelengths than at the higher preferred wavelengths, meaning that more energy must be applied to the fat in order to achieve the same level of heating. For example, almost 10 times the energy must be applied to the fat at 920 nm as at 1200 nm in order to achieve the same heating of the fat, and the heating increases by nearly another six times for the same energy at 1715 nm. At 2300 nm, the energy absorbed is about five times greater than at 1715. However, beyond 1300 nm, substantially all energy applied to water-rich tissue is absorbed in passing through several millimeters of skin, and it is therefore very difficult, even with pressure, for radiation at these

wavelengths to be used for non-invasively targeting subcutaneous fat, except possibly in areas such as sacks under the eyes or in the neck where this fat may be closer to the surface. Therefore, it is currently contemplated that radiation in the band around 1200 nm is the best compromise between energy reaching the subcutaneous fat through the overlying tissue and the radiation being of a wavelength which is absorbed sufficiently by the fat tissue to cause a
5 desired treatment to occur.

The mechanism by which the fat is destroyed or otherwise reduced will vary to some extent with the duration of radiation pulses and the temperature to which the fat is raised. If the fat cell temperature is raised slightly from body temperature of about 37°C by for example less
10 than 10°C, no lethal injury occurs to most of the cells. This temperature rise does however initiate a biochemical reaction or lipolysis in the fat cells causing the cells to metabolize fat, or accelerate the metabolization thereof, thereby reducing the level of fat. At higher temperatures, for a sufficient duration, depending on size, fat cells are killed. As with most dead cells, the body ultimately absorbs and disposes of these cells. At still higher temperatures, for example
15 above 60°C, the walls or membranes of the lipid cells, which walls are primarily of lipid-rich material, are blebed, losing their ability to encapsulate the liquid lipid therein, the liquid lipid leaking therefrom to form pools which will also ultimately be absorbed by the body. However, liquid lipid contains free fatty acid which, in sufficient quantity, can be toxic to the human body. Therefore, if a substantial pool of liquid lipid is formed in this way, it is preferable that
20 a hypodermic needle be inserted into this pool and that at least most of the liquid lipid be removed through the hypodermic needle so as to limit the amount thereof which is absorbed into the body. Typically, both because of the limited depth to which significant radiation can be applied in the subcutaneous fat layer and for other reasons, the blebed cells would generally only extend for a few millimeters into the subcutaneous fat layer, for example 2 to 3 mm.
25 Pooled liquid lipid may also be removed by perforating the skin above it and permitting it to drain or by facilitating drainage by manipulation/massage of the area or other techniques known in the art.

The advantage of the above procedure is that, so long as the temperature is kept low enough, for example below approximately 70°C or other collagen damage threshold, there will
30 be no damage to the collagen bands which hold the skin to the body, and in fact these bands may be contracted by the heat. This maintains skin tone, notwithstanding the removal of the underlying subcutaneous fat and reduces sagging skin or dimples in the treated skin area. While

if the temperature of fat cells was raised high enough, the lipid could be melted, eliminating the need for the body to either absorb it or for it to otherwise be removed, and such procedure is also within the contemplation of the invention, it is not currently believed to be a preferred procedure because of the damage to the collagen bands in the subcutaneous fat layer and other
5 problems which might occur at these elevated temperatures.

A possible procedure when using the teachings of this invention for ablating subcutaneous fat would be to place a cooling hand piece 32 in contact with the patient's skin, probably under at least some pressure, for a time sufficient to cool the skin to a desired level, perhaps 5 to 10 seconds. Because of hot blood flowing through the dermis, cooling generally
10 levels off after roughly this duration and cooling to greater depth is not achieved.

Once the precooling has been completed, the radiation source, for example the laser, is activated for an appropriate period of time, perhaps 1 to 100 seconds. The required fluence and pulse duration can be calculated or can be determined empirically by using microwave or ultrasonic depth measuring techniques or other techniques known in the art for measuring
15 temperature at depth. Another option is to insert a needle into the area where a liquid lipid pool should be formed if the heat was sufficient to bleb the cell membranes to see if a liquid pool has been formed. If a liquid pool has not been formed, then treatment is required at either a higher fluence or for longer duration. This procedure can be repeated until liquid lipid is obtained. The area from which the liquid lipid is being removed may be manually manipulated or
20 "milked" to facilitate the removal of the liquid lipid pool.

Since substantial fluence may be required in order to ablate subcutaneous fat in the manner indicated above because of both the energy loss in the overlying layers and the relatively low coefficient of absorption for the fat at the wavelengths which must be used to reach the subcutaneous fat, the head used for applying radiation should preferably utilize a
25 photorecycling technique, such as that taught in U.S. Patent No. 5,824,023 or in co-pending application Serial No. _____ filed March 12, 1999. In conjunction with photorecycling, another way of more efficiently getting energy to an area under treatment is to pinch a fold of skin containing the treatment area in a section of the radiation emitting head, facilitating the application of radiation to the treatment area from at least two directions. Such techniques are
30 taught, for example in U.S. Patent No. 5,735,844 and in co-pending application S.N. _____, the contents of which are incorporated herein by reference. Fig. 2B illustrates an embodiment 36 of the invention which practices this pinched-fold technique. For this embodiment, the head

is formed of an optically transparent dielectric material 37 such as sapphire or glass and has a plurality of optical fibers 38 affixed thereto or embedded therein which fibers are angled to impinge on a fold of skin 39 drawn into a recess 41 formed in material 37. Recess 41 might for example be ½ inch across. The head and recess may be relatively shallow with only the fibers 38 shown in the figure or the head and recess may extend for a selected width into Fig. 2B and additional fibers 38 may be provided at selected points along such width. A hole or groove 43 is provided to which negative pressure or vacuum may be applied to draw the fold of skin into groove 41 and a high reflecting coating 45 may be applied to the outer surface of material 37. Coating 45 is effective to retroreflect radiation exiting skin fold 39 back into the skin in a manner discussed in the prior patent/application to enhance energy efficiency, thus permitting more radiation to reach a desired site for the same energy from a radiation source. Optical fibers 38 can be angled to target a desired lipid-rich tissue region in fold 39.

While in the discussion above, required fluence has been more or less empirically determined, in some applications, the required fluence can be estimated by use of the following equation:

$$P = \frac{\rho_f \cdot c_f \Delta T \cdot d}{\left(1 - e^{-\frac{\tau}{\tau_1}}\right) \cdot \tau_1 \cdot (1 - e^{-\alpha_f d})} \quad (1)$$

Where P is power density, ΔT is temperature rise required from normal body temperature of approximately 37°C to achieve lipid heating in accordance with the selected technique discussed above, d is the size of the targeted lipid region, for example the diameter of a sebaceous gland or the depth in for example subcutaneous fat or fat surrounding an organ, vessel or the like which is to be targeted, τ_1 is a thermal relaxation time of the fatty tissue targeted, τ is pulse width, α_f is absorption coefficient of the fatty tissue, ρ_f is the density of the fat and c_f is the heat capacity of the fat. Fluence (E) is given by:

$$E = P\tau \quad (2)$$

Thermal relaxation time for fatty tissue can vary from several nanoseconds for lipid in the membrane of a cell, to seconds (for example for a sebaceous gland), to several hours (for example for subcutaneous fat).

Using the above equations, and assuming a temperature rise ΔT in the fat of approximately 13°C, to 50°C, the fluence required to be applied to the skin for a wavelength of 920 nm is 50-500 J/cm², the fluence required to be applied to the skin at 1200 nm is roughly 10-100 J/cm² and the fluence for 1715 nm is 1-50 J/cm². The low value in these ranges assumes the fat to be treated at substantially the skin surface with the fluence increasing as the depth of the fat being treated increases, the highest value being for subcutaneous fat at a depth of approximately 4 mm. Since at the other preferred wavelength band, radiation applied to the skin will not normally reach subcutaneous fat, for this wavelength band it has been assumed that the radiation is applied directly or nearly directly to the fat cells, differences in range being accounted for by differences in size or depth of the lipid cells being treated, pulse width and the temperature to which the fat is to be raised. With these assumptions, at 2300 nm, the fluence range is 0.5-20 J/cm².

Where the pulse duration is longer than the thermal relaxation time of the fat cells or tissues being heated, this being sometimes referred to as quasi-stationary heating, power densities required for selective damage of or initiation of biochemical processes in the fatty tissue are estimated to be in the following range:

920 nm: 500-2000 W/cm²

1200 nm: 50-500 W/cm²

1715 nm: 10-200 W/cm²

2300 nm: 5-50 W/cm²

The first three of these values are taken at the skin surface, while the last one is taken at the surface of the lipid tissue.

While in the discussion above, the sebaceous gland has been targeted for destruction as a treatment for acne, the sebaceous gland, being located close to the stem cells of a hair follicle, may be targeted for other therapeutic purposes. In particular, the fat in the sebaceous gland could serve as a chromophore which is preferably heated by radiation at one of the selected wavelengths, the heat from the sebaceous gland if at a relatively low level being sufficient to sever the hair shaft at the level of the sebaceous gland, which hairs may then be washed away. This would be the equivalent of a shave which might last several weeks. More intense targeting of the sebaceous gland could result in sufficient heating to destroy the stem cells of the follicle which could sufficiently damage or destroy the follicle to provide long term or even permanent hair removal. This technique would be particularly advantageous for people

having very light hair and light skin with little melanin in either the hair shaft or follicle, melanin being the chromophore normally used in other radiation hair removal techniques.

Another mechanism by which the teachings of this invention could be used for hair removal stems from the fact that papilla or bulb 23 is located in the upper regions of subcutaneous fat 16. Therefore, heating subcutaneous fat in the region of a hair follicle in the manner previously discussed will also result in a heating of the bulb/papilla of the hair follicle which can damage or destroy these structures. Damage or destruction of the bulb or papilla is another mechanism by which hair removal is effected.

The teachings of this invention may also be utilized to target lipid-rich tissue in other regions for other purposes. For example, the stratum corneum contains a layer of lipid tissue which serves as liquid barrier in a persons epidermis. This liquid barrier can reduce the effectiveness of needless injections which rely primarily on pressure to inject a liquid agent into the patient. A short burst of radiation at one of the wavelengths indicated above, for example 1715 nm or 2300 nm, could remove this lipid barrier in the area where the injection is to be made just prior to the injection to enhance the effectiveness thereof.

It is also known that the membranes walls of many cells are composed substantially of lipid and that these membranes differ somewhat from cell to cell. Radiation at one of the wavelengths indicated above may therefore be effective to selectively porate cells, the selectivity being achieved either as a result of controlling the focusing of the radiation to a targeted region and/or certain of the cells in the region porating at lower fluence or less time of radiation application than others as a result of cell size, wall thickness and/or other factors. Poration may be done for example to permit a drug or other therapeutic agent to enter the cell for healing or destruction thereof, for example, for the destruction of cancer cells, or to permit the content of the cell to flow out for various purposes. The poration may be temporary, or may be permanent resulting in cell destruction.

Finally, while in the discussion above the targeting of lipid as a chromophore for affecting hair removal in two different ways has been discussed, it is apparent that lipid could be targeted in other areas as a chromophore for the heating and either the destruction or therapy on other body components. Thus, in certain areas of the body, heating of lipid may be used to shrink collagen for wrinkle removal or skin toning or the lipid layer in the stratum corneum may be targeted for other purposes. Fat surrounding nerves, blood vessels or other biological structures may also be target for heating and treating the underlying structure. The radiation

wavelength, intensity, and pulse duration would in each instance be adjusted based on the size of the lipid structure being targeted, its depth, the wavelength utilized, and other factors.

Fig. 3 illustrates a technique which may be employed to treat subcutaneous fat either in areas where the dermis is too thick for treatment to be performed from the skin surface as shown in Fig. 2, where treatment is desired at depths in subcutaneous fat layer 16 which are too deep for treatment from the skin surface, where it is desired to operate at one of the more efficient longer wavelengths which do not normally penetrate to the subcutaneous fat, or for other reasons. In Fig. 3, a probe 40 is inserted through epidermis 12 and dermis 14 into subcutaneous fat region 16. Probe 40 may be a needle, or an opening may be formed in the skin through which a trocar or other cannula may be inserted, the probe 40 then passing through the cannula or trocar to the desired location. Other techniques known in the art for positioning a probe in subcutaneous fat region may be employed.

Probe 40 can contain an optical fiber or fiber bundle through which optical radiation at the wavelengths previously indicated may be applied to the end of the probe. The end of the probe may be formed to either direct the light straight ahead, to direct the light at some angle to the direction of the probe or to direct the radiation in more than one direction. Particularly where one of the longer wavelengths, for example 2300 nm, are utilized which have a high coefficient of absorption in fat, a dispersive lens might also be employed at the end of the needle to expend treatment area. A relatively large area of subcutaneous fat may be treated by a single insertion of the probe by moving the probe in and out of the subcutaneous fat and possibly by also rotating the probe about the entry point. Where light is coming out at an angle to the direction of the probe, the probe may also be rotated to cover a larger area. By inserting the probe at an angle as shown in Fig. 3, a larger area can be covered, though at a shallower depth. A smaller area to a greater depth can be covered by inserting probe 40 at a sharper angle. If the temperature to which the fat is raised by the radiations from the needle results in a liquid lipid pool being formed, a cannula could be included around the optical fiber in probe 40 to remove this liquid on a periodic or continuous basis, or the pool could be removed in the manner previously discussed. While the procedure of Fig. 3 may be used for any part of the body where fat is to be removed, it may be particularly advantageous for areas with smaller pockets of fat such as the face or neck. Further, while several techniques have been taught above for applying radiation within a preferentially absorbed wavelength band to subcutaneous

fat for the treatment thereof, other techniques, including various surgical techniques, could be utilized for reaching selected regions of subcutaneous fat in appropriate situations.

Another area where the teachings of this invention might be advantageously employed is to remove fat covering vessels, organs, or other anatomical elements on which a surgical procedure is to be performed so that the surgical procedure may be more accurately and safely performed with better visibility. In this instance, the tool for removing the fat might be inserted through a surgical opening or might be part of an endoscope or other tool inserted through a body cavity. The tool inserted could be similar to probe 40 and, to minimize damage to surrounding tissue, is preferably placed in contact with the fat to be treated, or at least in near contact with such fat, for irradiation. Thus, in Fig. 4 the tool is shown as a probe 50 inserted through a catheter 52 to the fat 54 surrounding a vessel, gut or other vital structure 56 to be surgically treated. Catheter 52 could also include a standard probe to permit viewing of the area under treatment so that catheter 52 can be repositioned and treatment can be continued until a sufficient amount of the fat 54 has been removed to expose vessel 56. Where larger surgical incisions are made, the tool for removal/treatment of fat 54 from vessel 56 might be hand held by the surgeon and manipulated by him to remove fat. Since fat 54 preferentially absorbs radiation at the applied wavelengths, and strongly absorbs at the higher wavelengths usable where there is substantial contact between the probe and the fat to be treated, the treatment of fat 54 should result in little if any thermal damage to underlying vessel 56 and, particularly if the wavelength is at approximately 1715 nm, or 2300 nm, this danger will be significantly reduced from prior art procedures where the radiation utilized was not preferentially absorbed by the fat tissue. More specifically, the fluence and exposure duration can be adjusted to ablate or otherwise treat fat, but not the nearby or underlying non-fat tissue.

A technique has thus been disclosed for the targeting of lipid-rich or fat tissue to effect a desired treatment by the selective application of optical radiation to such fat tissue at a wavelength preferentially absorbed thereby. While for various embodiments, the fat tissue for targeting has been discussed above, including the sebaceous gland, subcutaneous fat and fat surrounding anatomical elements on which surgical procedures are to be performed, the invention is not limited to targeting only such fat tissue, but may be employed for the targeting of any lipid-rich tissue. Further, while specific hardware has been described for producing radiation within the selected wavelength bands, other radiation sources capable of producing radiation within such bands might also be utilized. Finally, while specific methods and

hardware have been disclosed for applying the radiation to the various areas of lipid-rich tissue to be targeted, other techniques suitable for directing sufficient radiation at the requisite wavelengths to lipid-rich tissue may also be employed. Thus, while the invention has particularly been shown and described above with reference to preferred embodiments, the
5 foregoing and other changes in form and detail may be made therein by those skilled in the art without departing from the spirit and scope of the invention, which invention is to be limited only by the following claims.

1. A method for selectively targeting lipid-rich tissue to effect a desired treatment, said method comprising irradiating said lipid-rich tissue with optical radiation at a wavelength for which absorption coefficients for fat and water have a ratio which is at least 0.5, the radiation
5 being at a fluence and for a duration sufficient for the desired treatment.
2. A method as in claim 1 wherein said ratio is at least 1.
3. A method as in claim 1 wherein said wavelength is in a band which is one of (a) 880 to
10 935 nm, (b) 1150 to 1230 nm, (c) 1690 to 1780 nm, and (d) 2250 nm to 2450 nm.
4. A method as claimed in claim 3 wherein the wavelength is in a band which is one of 900 nm to 930 nm, 1190 to 1220 nm, 1700 nm to 1730 nm, and 2280 nm to 2360 nm.
- 15 5. A method as claimed in claim 4 wherein said wavelength is one of approximately 920 nm, 1210 nm, 1715 nm, 2300 nm and 3375 nm.
6. A method as claimed in claim 3 wherein said fluence varies as a function of a number of factors including the wavelength band utilized and the size of the lipid-rich tissue being
20 treated.
7. A method as claimed in claim 3 wherein said fluence is approximately 0.5 J/cm² to 500 J/cm².
- 25 8. A method as claimed in claim 3 wherein said duration is approximately 4 fs to several minutes.
9. A method as claimed in claim 3 wherein the lipid-rich tissue is at least one sebaceous gland.
- 30 10. A method as claimed in claim 9 wherein irradiating said tissue is performed by applying said energy to the skin surface overlying the at least one sebaceous gland.

11. A method as claimed in claim 10 wherein the wavelength is in one of band (b), (c), and (d).

12. A method as claimed in claim 3 wherein said lipid-rich tissue is subcutaneous fat.

5

13. A method as claimed in claim 12 wherein irradiating said tissue is performed by applying said energy to the skin surface overlying the subcutaneous fat to be treated.

14. A method as claimed in claim 13 wherein the wavelength is in one of band (a) and band (b).

10

15. A method as claimed in claim 13 wherein said energy is applied through an applicator applying pressure to skin above said subcutaneous fat to be treated.

16. A method as claimed in claim 13 including cooling the skin above the subcutaneous fat to be treated to a selected depth.

15

17. A method as claimed in claim 16 wherein said selected depth is in the dermal layer of said skin.

20

18. A method as claimed in claim 13 wherein a fold of skin containing subcutaneous fat to be treated is drawn into a slotted head and irradiated from at least two sides.

19. A method as claimed in claim 12 wherein irradiating said tissue is performed by applying said energy through a probe passed through the skin to the region of subcutaneous fat to be treated.

25

20. A method as claimed in claim 19 wherein said probe is passed into the subcutaneous fat at an angle to the skin surface, and including performing at least one of moving the probe in and out of the skin and rotating the probe about its skin entry point to irradiate and treat subcutaneous fat over a selected area.

30

21. A method as claimed in claim 19 including removing liquid fat formed as a result of the irradiation ablating lipid tissue walls through a cannula included as part of said probe.

22. A method as claimed in claim 12 wherein the radiation applied to said subcutaneous fat tissue is of sufficient fluence and duration to ablate walls of such tissue to form a liquid fat pool.

23. A method as claimed in claim 22 including inserting a needle into said pool, and
5 removing liquid fat from said pool through said needle.

24. A method as claimed in claim 22 including said pool being absorbed into a patient's body.

10 25. A method as claimed in claim 22 including draining said pool through an opening in the patient's skin.

26. A method as claimed in claim 3 including focusing radiation to a treatment area in the subcutaneous fat.

15

27. A method as claimed in claim 22 wherein said fluence and duration are such that ablations of tissue walls occurs only to a selected depth in said subcutaneous layer.

28. A method as claimed in claim 3 wherein said lipid-rich tissue is fat surrounding an
20 anatomical element on which a surgical procedure is to be performed, and wherein irradiating said tissue is performed by a tool in at least near contact with the fat to remove the fat from and thereby expose the element.

29. A method as claimed in claim 27 wherein said wavelength is in one of bands (b), (c),
25 and (d).

30. A method as claimed in claim 3 wherein said treatment is achieved photomechanically, and wherein said duration is less than 1 μ s.

30 31. A method as claimed in claim 3 wherein said lipid-rich tissue is heated to heat and treat tissue adjacent thereto.

32. A method as claimed in claim 31 wherein said lipid-rich tissue a sebaceous gland, heating of the sebaceous gland effecting hair removal.

33. A method as claimed in claim 32 wherein said lipid-rich tissue a subcutaneous fat,
5 heating of the subcutaneous fat effecting hair removal.

34. A method as claimed in claim 3 wherein said lipid-rich tissues a cell membrane, heating of the cell membrane selectively porating the cell.

10 35. Apparatus for selectively targeting lipid-rich tissue to effect a desired treatment, said apparatus including:

a source of radiation at a wavelength for which absorption coefficients for fat and water have a ratio which is at least 0.5, said source when energized, providing the radiation at a fluence and for a duration sufficient for the desired treatment; and

15 a component which delivers the energy from said source to the lipid-rich tissue to be treated.

36. Apparatus as claimed in claim 35 wherein said ratio is at least 1.

20 37. Apparatus as claimed in claim 35 wherein said wavelength is in a band which is one of (a) 880 to 935 nm, (b) 1160 to 1230 nm, (c) 1690 to 1780 nm, and (d) 2250 nm to 2450 nm.

38. Apparatus as claimed in claim 37 wherein the wavelength is in a band which is one of 900 nm to 930 nm, 1190 to 1220 nm, 1700 nm to 1730 nm, and 2280 nm to 2350 nm.

25

39. Apparatus as claimed in claim 37 wherein said fluence is approximately 0.5 J/cm² to 500 J/cm.

40. Apparatus as claimed in claim 37 wherein said source is a potassium cadmium laser with
30 a matrix KCd(WO₄)₂ which is doped with Er³⁺ ions, with an orientation such that the axis of the laser beam is at an angle greater than 45 degrees with the crystalline axis [010], the source generating an output at approximately 1715 nm.

41. Apparatus as claimed in claim 37 wherein the component is an applicator adapted to be in pressure contact with skin above the lipid-rich tissue to be treated.

42. Apparatus as claimed in claim 37 wherein said energy is applied to the lipid-rich tissue to be treated through overlying skin, and wherein the component includes a mechanism which cools said overlying skin to a selected depth.

43. Apparatus as claimed in claim 37 wherein said component is a probe applied through skin overlying the lipid-rich tissue to be treated to a region containing such tissue.

10

44. Apparatus as claimed in claim 43 wherein said probe includes a cannula through which liquid fat formed as a result of the irradiation ablating lipid tissue walls is removed.

45. Apparatus as claimed in claim 37 including a cannula inserted into a pool of liquid fat formed as a result of the irradiation melting lipid tissue walls to remove the liquid fat.

15

46. Apparatus as claimed in claim 37 including a slotted head for irradiation delivery, and a mechanism for drawing a fold of skin to undergo said desired treatment into said slot of said head.

48. Apparatus as claimed in claim 37 wherein said component is a tool which is adapted to be brought into at least near contact with lipid-rich tissue surrounding an anatomical element on which a surgical procedure is to be performed.

20

49. Apparatus as claimed in claim 37 wherein said fluence is approximately 0.5 J/cm² to 500 J/cm², depending on a number of factors including wavelength band utilized and size of the lipid-rich tissue being treated.

25

50. Apparatus as claimed in claim 37 wherein said duration is approximately 4 fs to several minutes.

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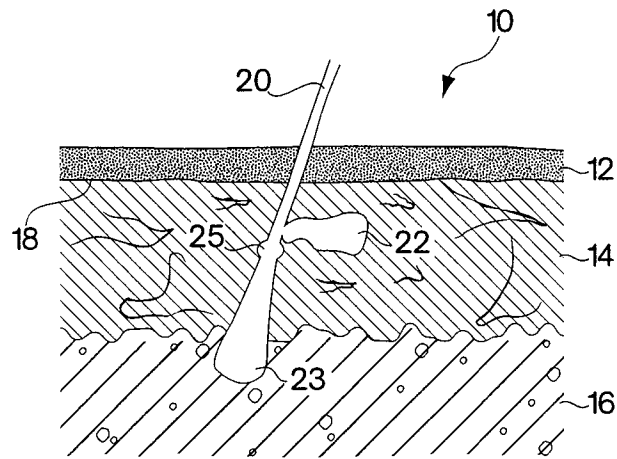


Fig. 1

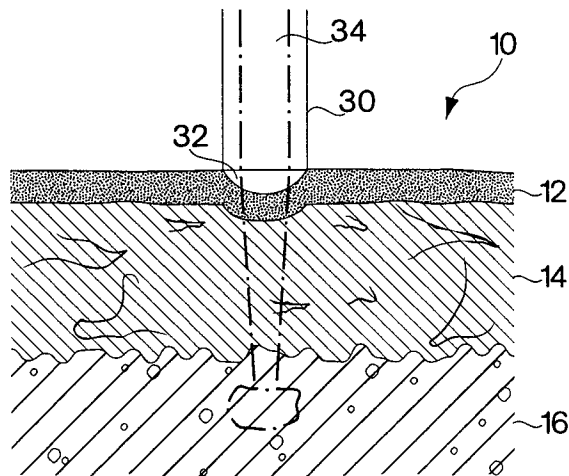


Fig. 2A

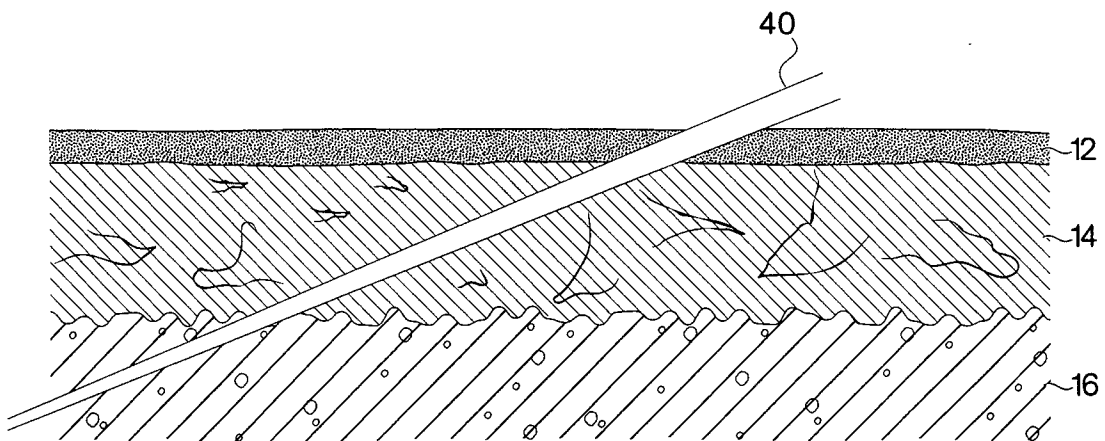


Fig. 3

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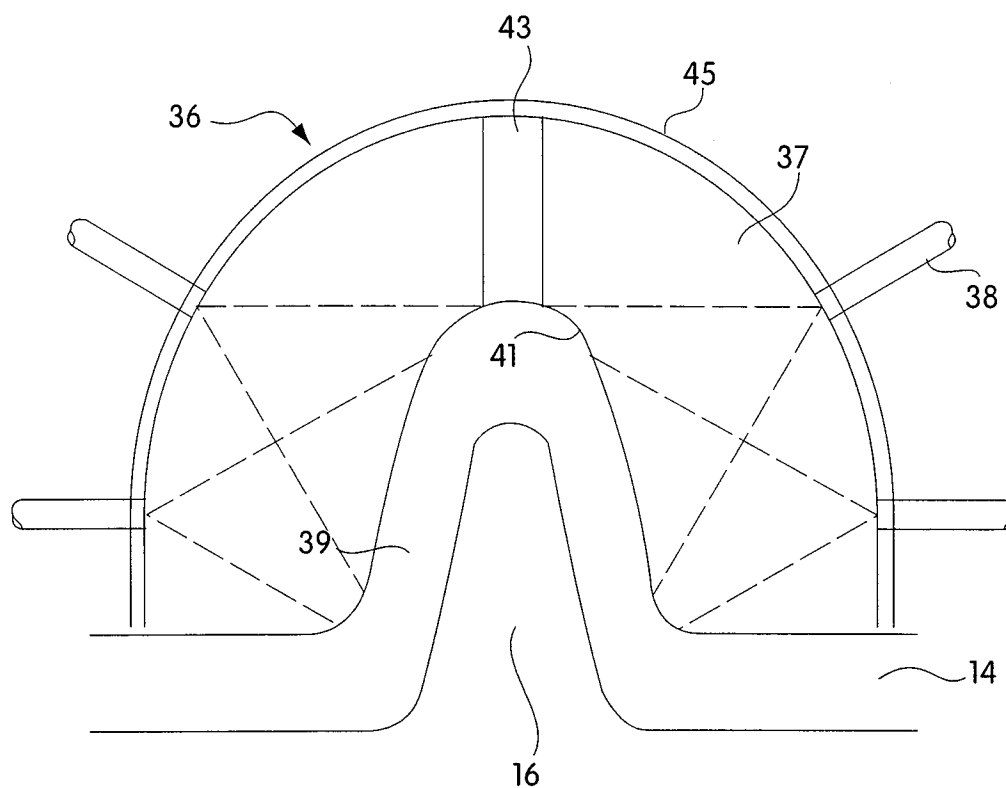


Fig. 2B

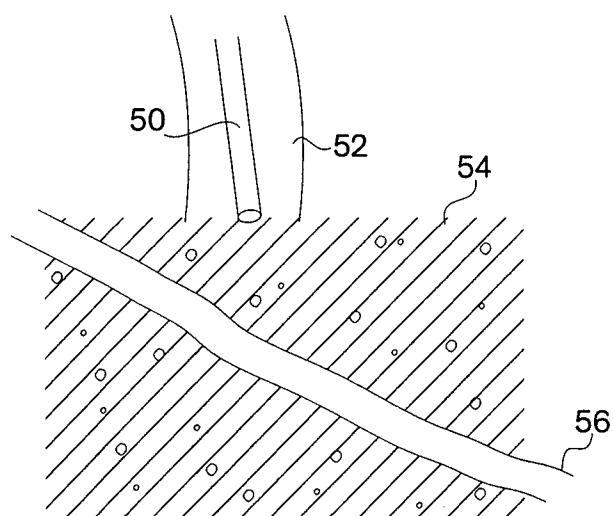


Fig. 4

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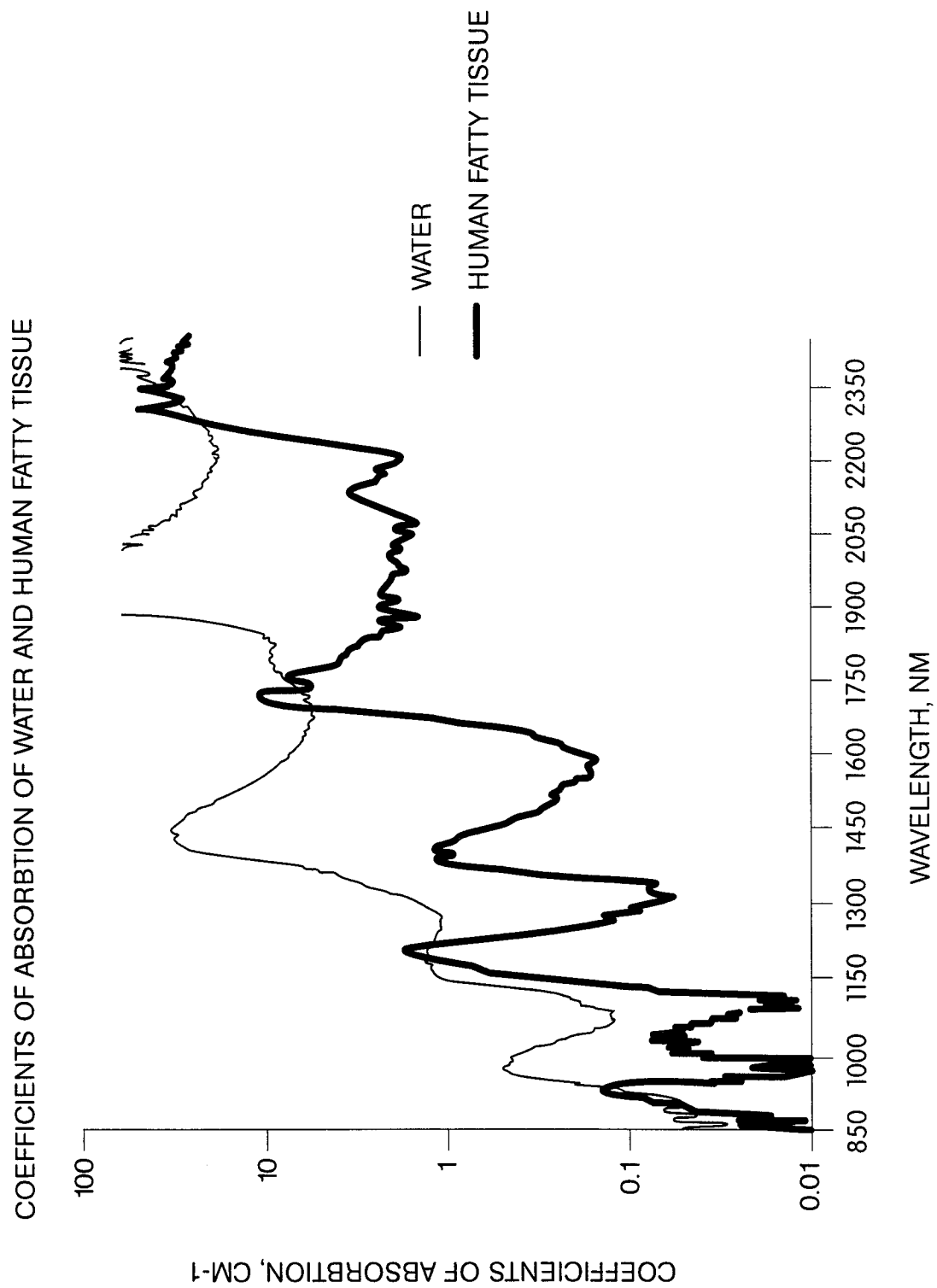


Fig. 5

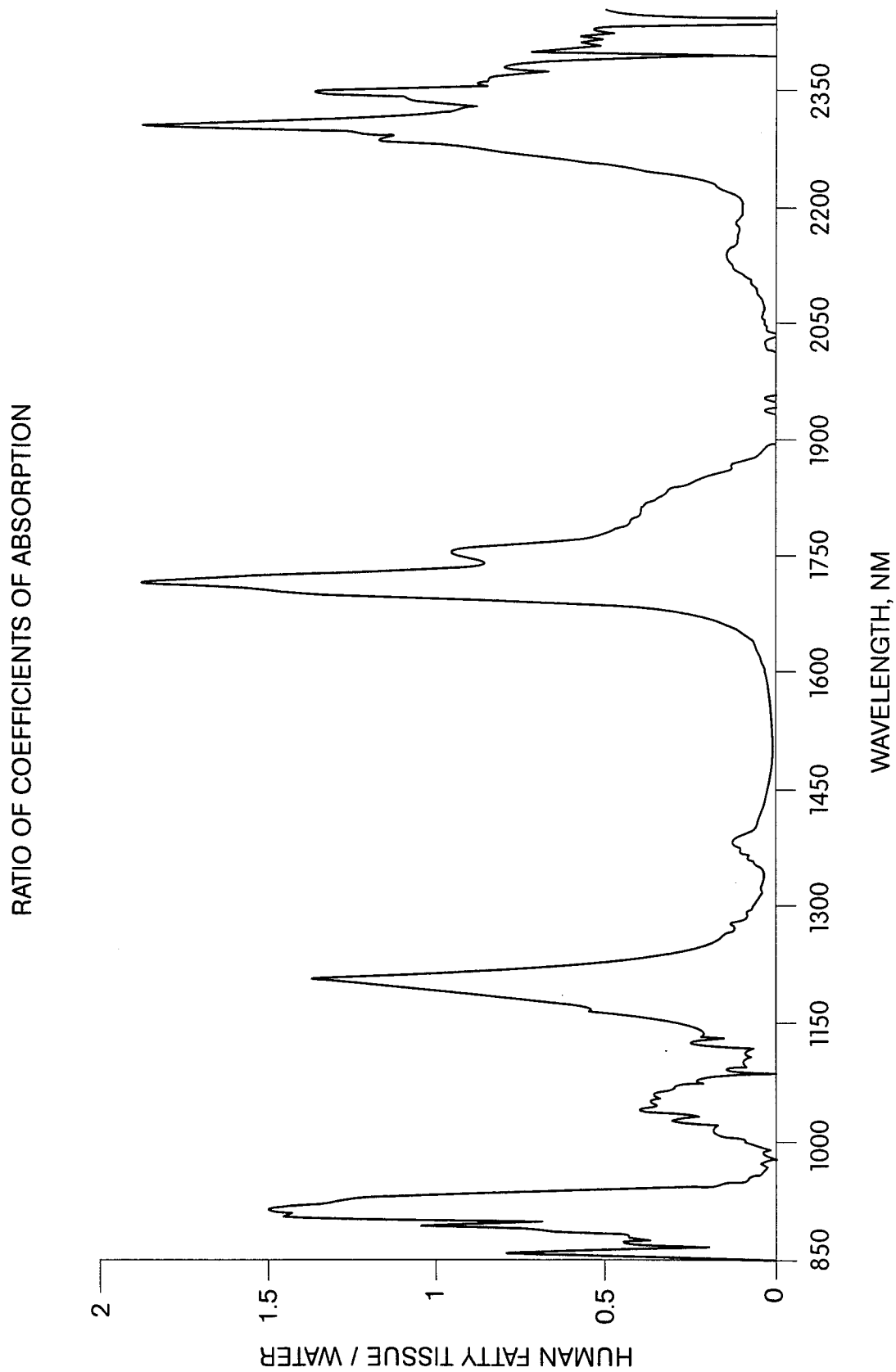


Fig. 6

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/06475**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(6) :A61N 5/06

US CL :606/009

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 606/002, 003, 7, 8, 10-12, 14-18

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

APS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y,P	US 5,817,089 A (TANKOVICH et al.) 06 October 1998, entire document.	1, 2, 35, 36
Y	US 5,304,170 A (GREEN) 19 April 1994, entire document.	1, 2, 35, 36
A	US 5,403,306 A (EDWARDS et al.) 04 April 1995.	1-50
A	US 5,655,547 A (KARNI) 12 August 1997.	1-50
A	US 5,505,727 A (KELLER) 09 April 1996.	1-50

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

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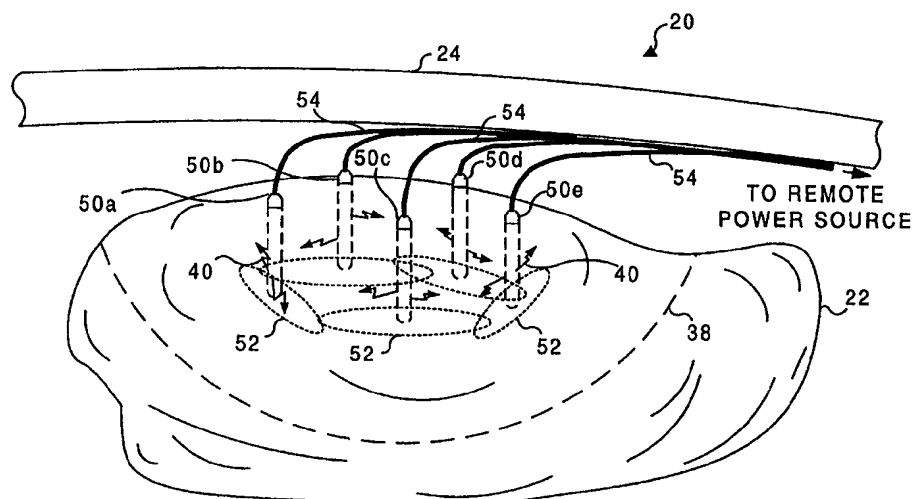
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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(21) International Application Number: PCT/US99/09582 (22) International Filing Date: 30 April 1999 (30.04.99) (30) Priority Data: 09/103,761 24 June 1998 (24.06.98) US (71) Applicant: LIGHT SCIENCES LIMITED PARTNERSHIP [US/US]; 1065 – 12th Avenue N.W. #E5, Issaquah, WA 98027 (US). (72) Inventor: CHEN, James, C.; 2011 – 87th PL N.E., Bellevue, WA 98004 (US). (74) Agent: ANDERSON, Ronald, M.; Law Offices of Ronald M. Anderson, Suite 507, 600 – 108th Avenue, N.E., Bellevue, WA 98004 (US).		(81) Designated States: AU, CA, JP, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). Published With international search report. With amended claims.

(54) Title: APPLICATION OF LIGHT AT PLURAL TREATMENT SITES WITHIN A TUMOR TO INCREASE THE EFFICACY OF LIGHT THERAPY



(57) Abstract

Light is administered during photodynamic therapy (PDT) for an extended period of time at a plurality of sites (52) distributed within the abnormal tissue of a tumor (22). A clinical study has shown that a substantially greater volume of abnormal tissue in a tumor is destroyed by the extended administration of light therapy from a plurality of probes (50a-50e) than would have been expected based upon the teaching of the prior art. In this process, a plurality of light emitting optical fibers or probes are deployed in a spaced apart array. The greater volume of necrosis (38) in the tumor (22) is achieved due to one or more concomitant effects, including the inflammation of damaged abnormal tissue, and resultant immunological response of the patient's body; and the collapse of the vascular system that provides oxygenated blood to portions of the tumor outside the expected fluency zone.

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APPLICATION OF LIGHT AT PLURAL TREATMENT SITES WITHIN A TUMOR TO INCREASE THE EFFICACY OF LIGHT THERAPY

Field of the Invention

The present invention generally relates to the use of light therapy to
5 destroy abnormal tissue in a tumor, and more specifically, to the use of multiple
light sources disposed at spaced-apart treatment sites within a tumor to render the
therapy.

Background of the Invention

Abnormal tissue in the body is known to selectively absorb certain dyes
10 that have been perfused into a treatment site to a much greater extent than
surrounding tissue. For example, tumors of the pancreas and colon may absorb
two to three times the volume of these dyes, compared to normal tissue. Once
pre-sensitized by dye tagging in this manner, the cancerous or abnormal tissue can
be destroyed by irradiation with light of an appropriate wavelength or waveband
15 corresponding to an absorbing wavelength or waveband of the dye, with minimal
damage to normal tissue. This procedure, which is known as photodynamic
therapy (PDT), has been clinically used to treat metastatic breast cancer, bladder
cancer, lung carcinomas, esophageal cancer, basal cell carcinoma, malignant
melanoma, ocular tumors, head and neck cancers, and other types of malignant
20 tumors. Because PDT may selectively destroy abnormal tissue that has absorbed
more of the dye than normal tissue, it can successfully be used to kill the
malignant tissue of a tumor with less effect on surrounding benign tissue than
alternative treatment procedures.

The effectiveness of PDT for treating tumors has become increasingly
25 more evident to the medical community. Each year, numerous papers are
published disclosing research that has been carried out to explore how PDT can
more effectively be used and to better understand the processes by which PDT
destroys abnormal cells. Much of the prior art discloses the use of relatively high
powered lasers as an external light source employed to administer the light to a

treatment site. Typically, the light from an external laser source is conveyed through an optical fiber to a treatment site on the skin of a patient or to an internal site within the patient's body. Penetration of a tumor by the optical fiber is achieved either through a small incision in the overlying dermal layer, or directly, if the tumor is surgically exposed.

Most applications of PDT are conducted using a single optical fiber to provide the light therapy. An optical fiber used to render PDT may include a diffuser on its distal end to enhance the radial distribution of light from the fiber. Light emitted through the diffuser more fully illuminates a treatment site within a tumor in which the optical fiber has been inserted.

Research has been conducted to measure the penetration depth of light into tissue as a basis for assessing the volume of tissue that will be affected by the light applied to a treatment site to render PDT. This research has determined that the penetration depth (or a reciprocal value corresponding to the light attenuation of the tissue) depends upon the wavelength of the light, the type of tissue, the direction of irradiation, the oxygenation of the tissue, the striation of the tissue, the perfusion of blood in the tissue at the site, and other physiological and physical factors. Generally, at a wavelength of about 630 nm, the depth of penetration of light into tissue has been found to be between about 0.2 mm and 7 mm, depending upon the type of tissue (as reported in "*In Vivo* Measurement of the Optical Interaction Coefficients of Human Tumors at 630 nm," I. Driver, C.P. Lowdell, and D.V. Ash, *Phys. Med. Biol.*, Vol. 36, No. 6, pp. 805-813, Table 3, (1991). Further, this paper reported a large inter-sample variation for the depth of light penetration in the same type of tissue. Tissue of a darker color, such as that of the liver, greatly attenuates light transmission, while brain tissue tends to scatter the light and thus limits light penetration. Generally, longer wavelength light penetrates more deeply, but most of the currently available photoreactive reagent dyes used for PDT have absorption wavebands in the 600-700 nm range.

The limited penetration depth of light in tissue would seem to indicate that light emitted at a single treatment site to render PDT will be effective in destroying abnormal tissue in only a relatively small volume within a tumor. To treat larger tumors, multiple light treatment sites would be expected to linearly expand the volume as a function of the number of light treatment sites used, i.e., the total volume of the effective zone in a tumor treated with the multiple optical fibers should be equal to the product of the volume treated at one site and the number of sites. In a paper entitled "Photodosimetry of Interstitial Light Delivery

to Solid Tumors," M.C. Fenning, D.Q. Brown, and J.D. Chapman, Medical Physics, Vol. 21, No. 7, pp. 1149 – 1156 (July 1994), reported on research in which both anaplastic and well-differentiated Dunning prostate adenocarcinomas were illuminated in anesthetized Fisher X Copenhagen rats by light from single-fiber and multiple-fiber illuminators. Each illuminator consisted of a 2 cm laterally diffusing optical fiber placed within a plastic brachytherapy needle implanted into a tumor. The radial falloff of intensity with distance from single fibers was used to determine light attenuation coefficients for various wavelengths, by employing a two-dimensional (2D) photodosimetry computer code. The coefficients were used to calculate relative light intensities in planes perpendicular to the single-fiber and various multiple-fiber configurations. Relative light intensities measured along tumor tracks were compared with those predicted by the 2D photodosimetry evaluation and were found to agree within $\pm 14\%$, for all configurations of the optical fibers studied. It was noted that at wavelengths equal to and greater than about 700 nm, optical fiber spacings of at least one cm produced relatively uniform light fields ($\pm 20\%$) in tumor planes perpendicular to the optical fibers. At line 32 of the second column on page 1155 of the paper, it is noted that:

For human tumors with light attenuating properties similar to the R3327-H tumor, the heterogeneity of light dose in tumor volumes delivered by a multifiber illuminator with 1.0-cm spacings will be considerably greater than $\pm 20\%$. Illumination of tumors by such procedures will produce relatively large variations in biological effect by interstitial PDT. Furthermore, to expose all tumor tissue to a minimum light dose required for a specific biological effect, large fractions of the tumor would of necessity be overdosed. While this may not seriously impact upon tumor response, it will limit the volume of solid tumor which can be treated with a specific time by a specific light source. Laser output intensity has not been a limiting factor for the illumination of superficial lesions in clinical studies to date. Nevertheless, to successfully scale up this procedure for the treatment of bulky human tumors, laser output intensity and tumor volume will determine the time required to deliver a curative light dose.

The paper further concludes that more than seven optical fibers may be required to properly treat a tumor with PDT, to guarantee that adequate light is delivered, particularly to the periphery of a tumor, due to the rapid falloff of light at the edge of the illuminated field. The reference thus teaches or suggests that the effect of

PDT on a human tumor, particularly one of larger size, will be limited to the region of the tumor directly viably illuminated by the plurality of optical fibers and implies that it will be necessary to repeat the treatment to different areas of the tumor by moving the plurality of the optical fibers so that direct illumination of a greater treatment volume can be accomplished.

The effects of PDT and the manner in which it destroys tissue are not clearly understood. It is believed that the primary mechanism by which PDT destroys cells relies upon the conversion of molecular oxygen to singlet oxygen and the release of free radicals by the light activated dye. In "How Does Photodynamic Therapy Work?" by B.W. Henderson, and T.J. Dougherty, Photochemistry and Photobiology, Vol. 55, No. 1, pp. 145-157 (1992), it is noted that following the absorption of light, a sensitizer is transformed from its ground state to an excited triplet via a short-lived singlet state. The excited triplet can react directly either with a substrate or solvent by hydrogen atom or electron transfer to form radicals and radical ions (Type I reaction) or it can transfer its energy to oxygen directly to form singlet oxygen, which is a highly reactive species (Type II reaction). The paper states that indirect evidence suggests singlet oxygen is the major damaging species in PDT. Based on this belief, the reference concludes that PDT effects should be oxygen-dependent, with full effects of PDT being observed *in vitro* at oxygen concentrations of about 5%. It is reported by the reference that "no photosensitization can be observed in the absence of measurable oxygen." Further, the reference teaches that the diffusion distance of singlet oxygen in cells is about 0.1 μm , so that cell damage caused by singlet oxygen will occur close to its locus of generation. Singlet oxygen causes a loss of cell integrity by a photoperoxidation of membrane cholesterol and other unsaturated phospholipids. Associated with the cell membrane damage is a release of inflammatory and immune mediators. Also released through mast cell degranulation is histamine. The substances released are vasoactive, either constrictive or dilatory, and it is believed that they induce vascular damage. Tumor necrosis factor (TNF) is also released, and it too can cause vascular damage. The degree of vascular photosensitivity in tissue appears to be a function of the level of the circulating photoreactive agent. This reference reports that vascular damage in a tumor microenvironment induces hypoxic tumor cell fractions. A key conclusion stated in the paper is that the "rapid shift of cells into hypoxia [after PDT], where they are protected from further PDT damage due to the oxygen limitation of the photodynamic processes, is potentially limiting to

direct tumor cell photodestruction.” In essence, this statement indicates that efficacy of PDT in destroying tumor cells quickly diminishes after the light activation due to the self limiting effects of hypoxia caused by photovascular occlusion. In other words, the paper concludes that the resulting vascular
5 occlusion limits further blood flow to the treatment site, which is necessary to supply additional molecular oxygen to the tumor cells for use in generating more singlet oxygen.

Also reported in the last cited reference is an observed infiltration of PDT-treated tissue with lymphocytes, plasma cells and histiocytes, which suggests an
10 immune response to effects of the PDT. In high dose bladder PDT treatments, high levels of interleukin 1-beta, interleukin 2, and TNF-alpha have been observed in patients’ urine for up to 50 days following the therapy, concurrent with severe inflammatory symptoms. The relative extent of abnormal cell necrosis caused by generation of singlet oxygen and free radicals compared to that resulting from the
15 immune response is not clear from the prior art.

It has been shown that illuminating abnormal cells, which have absorbed a photoreactive agent, with relatively low levels of light for extended periods of time may be even more effective in rendering PDT than the more conventional approach of using a high intensity laser light source to administer light for short
20 time intervals. In commonly assigned U.S. Patent No. 5,445,608, a plurality of transcutaneously implantable probes that include relatively low intensity light sources are disclosed for rendering PDT to treatment sites within a patient’s body. Such probes can be implanted interstitially within a tumor to administer PDT for many hours or days. As necessary, repetitive infusions of a suitable photoreactive
25 agent can be made to sensitize the abnormal cells comprising the tumor so that they are susceptible to being destroyed by the PDT. An apparent question arises in regard to the efficacy of such an approach to treating a relatively large tumor. In view of the teaching of the art discussed above, one would be led to conclude that low intensity light sources on an interstitial probe would lack adequate
30 penetration into a large tumor mass to treat more than a relatively small portion of the tumor – even if plural probes of this type were used. In addition, the prior art suggests that extended PDT delivered to a treatment site will not be effective in a large tumor due to the hypoxia resulting from vascular damage and the vasculature constriction that occurs soon after the PDT commences.

35 Application of PDT to a larger tumor would seem to require that a plurality of optical fibers spaced sufficiently close together and of sufficient

number be inserted into the tumor to ensure that the light intensity between the optical fibers is substantially uniform throughout the volume of the tumor being treated. However, in view of the teaching of the prior art, implanting sufficient numbers of optical fibers or low light intensity probes to provide such uniform illumination does not seem to be a practical approach for treating a larger tumor. The expected effective zone of PDT would seem to be too limited due to the relatively shallow penetration of light into the tissue to justify the use of PDT to treat a large tumor.

Summary of the Invention

Contrary to the suggestion of the prior art, it appears that PDT can be successfully used for treating larger tumor masses, and that the depth of light penetration into tumor tissue when effecting PDT is not so limiting as indicated in the prior art, in determining the true extent of the effectiveness of the therapy. Indeed, the effective zone of PDT in large tumors has been found to be much larger than the volume of the tumor into which light administered has previously been found to penetrate. Furthermore, the effectiveness of the PDT in treating a larger volume of a tumor appears to be more dependent upon a pattern in which light emitting sites are arrayed in the tumor than previously known.

In accord with the present invention, a method is defined for destroying abnormal tissue in a tumor within a patient's body using an extended light therapy and at least one concomitant effect thereof. The method includes the step of administering a photoreactive agent to the abnormal tissue. The photoreactive agent, which has a characteristic absorption waveband, is preferably absorbed by the abnormal tissue rather than by normal tissue in the patient's body. Light having a waveband corresponding to the absorption waveband of the photoreactive agent is administered to a treatment zone in the tumor. A pattern in which the light is administered to the tumor defines the treatment zone, and this zone preferably encompasses a substantial portion of the tumor not penetrated by the light being administered. The method provides for continuing to administer the light to the treatment zone for at least three hours of extended light therapy. The light destroys the abnormal tissue that it illuminates by activating the photoreactive agent absorbed thereby. Furthermore, the extended period of light therapy indirectly destroys the substantial portion of the tumor that is not penetrated by the light being administered by inducing at least one concomitant effect that destroys the abnormal tissue comprising the substantial portion of the tumor.

In one case, the concomitant effect arises because the destruction of the abnormal tissue in the treatment zone deprives the substantial portion of the tumor from receiving oxygen. The abnormal tissue in the substantial portion of the tumor is thus destroyed due to oxygen depletion.

5 In another instance, the concomitant effect arises because the photoreactive agent within the treatment zone that is activated by the light being administered diffuses into the substantial portion of the tumor that is not penetrated by the light. This photoreactive agent that is thus activated then destroys the abnormal tissue in the substantial portion of the tumor not directly
10 penetrated by the light.

 In yet another instance, the concomitant effect arises because the light therapy causes necrosis of the abnormal tissue in the treatment zone, which causes either an immune response or an inflammation in the patient's body that destroys the abnormal tissue in the substantial portion of the tumor not directly penetrated
15 by the light.

 In still another instance, the concomitant effect arises because the destruction of abnormal tissue in the treatment zone causes either a vascular collapse, stasis, or occlusion, so that blood flow to the substantial portion of the tumor that is not directly penetrated by the light is terminated, causing the
20 abnormal tissue in that substantial portion to die.

 In one embodiment of the method, the light is administered through an optical fiber from a source that is external to the patient's body. The method further preferably includes the step of implanting a plurality of probes for administering the light into the tumor at spaced-apart locations within the
25 treatment zone. In one embodiment, the light is then administered from at least one light source included on each of the plurality of probes. In another embodiment, the light is delivered to the plurality of probes through a plurality of optical fibers from a source that is external to the patient's body. The treatment zone is not more than about 3 cm from each of the plurality of probes.

30 In the method, the light administered to the treatment zone produces singlet oxygen, which depletes oxygen from the substantial portion of the tumor that is outside the treatment zone, causing a gradient of hypoxia and anoxia in that portion of the tumor, which leads to a destruction of the abnormal tissue contained therein.

35 The method may include further steps. Specifically, in one embodiment, the light is emitted into the tumor in a first direction from each of the plurality of

probes, relative to the probe from which the light is emitted. Next, the method provides for terminating emission of light into the tumor in the first direction and emitting light into the tumor in a second direction from each of the plurality of probes. The second direction is substantially different from the first direction for each of the probes. Preferably, in one embodiment, the first direction is directed toward a perimeter of the tumor, and the second direction is directed toward an interior of the tumor. By first destroying the perimeter of the tumor, the interior portion of the tumor is more readily destroyed due to the one or more concomitant effects.

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Brief Description of the Drawing Figures

The foregoing aspects and many of the attendant advantages of this invention will become more readily appreciated as the same becomes better understood by reference to the following detailed description, when taken in conjunction with the accompanying drawings, wherein:

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FIGURE 1 is a schematic drawing illustrating a side elevational view of a first embodiment of the present invention for administering light to a treatment site within a tumor in a patient's body;

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FIGURE 2 is a plan view of the tumor shown in FIGURE 1, illustrating the positions of probes and the radial depth to which light emitted thereby directly penetrates into the tumor;

FIGURE 3 is a side elevational view of a second embodiment of the present invention, showing the tumor with a plurality of light emitting implanted probes inserted therein;

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FIGURE 4 is a plan view of the tumor shown in FIGURE 3, illustrating the direct light penetration pattern for each of the probes;

FIGURES 5A – 5C are three different embodiments of light emitting probes having a plurality of light sources contained therein;

FIGURES 6A and 6B illustrate two different embodiments of an optical fiber probe that emits light in only a preferred direction;

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FIGURE 7 is a schematic diagram comparing a depth of direct light penetration in a tumor to a depth of tumor necrosis caused by one or more secondary effects;

FIGURE 8 is a plan view of a tumor showing a plurality of probes that selectively emit light in one of two different directions;

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FIGURE 9 is an electrical schematic diagram of a circuit that selectively energizes one of two different groups of light emitting diodes (LEDs);

FIGURE 10 is a plan view showing an alternative embodiment in which light from two different groups of light sources within each of a plurality of probes is selectively energized;

5 FIGURE 11A is a schematic side elevational view of a retroperitoneal tumor within a patient's body that was treated in accord with the present invention;

10 FIGURE 11B is a plan view of the tumor of FIGURE 11A showing the disposition of a plurality of probes used to administer PDT to the tumor, the expected fluence zone, and the substantially greater expanded necrotic zone actually achieved;

FIGURE 12 is a side elevational view of a first pattern of light emitting probes for enhancing the effect of PDT in treating a large volume tumor; and

FIGURE 13 is a side elevational view of a second pattern of light emitting probes for enhancing the effect of PDT in treating the large volume tumor.

15 **Description of the Preferred Embodiment**

With reference to FIGURE 1, the present invention is illustrated in connection with treating a tumor 22 that is disposed within a patient's body 20. Tumor 22 is relatively large, having a length of approximately 7 to 10 cm and a transverse width of about 7 cm in this exemplary illustration. The tumor is
20 disposed below a dermal layer 24, for example, within the patient's abdominal cavity.

In the present invention, PDT plays an important role is destroying abnormal tissue comprising tumor 22. As is done when rendering conventional PDT, a photoreactive agent is administered to the patient either orally or by
25 injection and is selectively preferentially absorbed by the abnormal tissue of tumor 22. Thereafter, using a surgical procedure to access tumor 22 through dermal layer 24, or using an endoscopic procedure with minimally invasive impact, a plurality of optical fibers 30a-30e are inserted into the interior of tumor 22 in a spaced-apart array so that the optical fibers are arranged in a pattern
30 that is more likely to increase the effectiveness of the therapy administered to the tumor. A laser light source 26 produces light lying within the light absorption waveband of the photoreactive agent that has been administered to the patient.

Light emitted by laser light source 26 is conveyed through an optical fiber 27 to a splitter 28 that divides the coherent light so that it is equally
35 distributed among optical fibers 30a-30e. The light is conveyed through these optical fibers toward their distal ends. Optical fibers 30a-30e include an outer

cladding 32 that minimizes losses through the outer surface of the optical fiber, insuring that substantially all of the light input to the optical fibers at their proximal ends, i.e., at splitter 28, is conveyed through the optical fibers to their distal ends, which have been inserted interstitially into the interior of tumor 22.

5 In the embodiment illustrated in FIGURE 1, cladding 32 is removed from approximately the last 3 to 4 cm of the distal ends of each of optical fibers 30a-30e, exposing a core 34. A diffusing surface is provided on the exposed portion of core 34, e.g., by roughening the surface of the exposed core, thereby insuring that light conveyed through the optical fibers is uniformly
10 distributed through the sides and through the distal ends of the optical fibers inserted into the tumor. Light emitted by the exposed distal ends of each of these optical fibers penetrates tumor 22 to an effective depth of less than 1.5 cm. The penetration depth of the emitted light into the tumor determines a generally cylindrical expected fluence zone 36, the radius of which is indicated by the dotted circles shown in FIGURE 1, and more clearly, in the plan view of
15 FIGURE 2.

As will be evident from FIGURE 2, the exposed portions of cores 34 from which the cladding has been removed are inserted into tumor 22, generally forming a circle in which the expected fluence zones 36 around each optical fiber at least partially overlap. It should also be noted that the expected fluence zone
20 for each optical fiber is determined partly by the intensity of the light delivered to the distal ends of each of the optical fibers and partly by the nature of the abnormal tissue in tumor 22. Measurements in the prior art indicate that for most tumor tissue, the maximum effective depth of light penetration (at a wavelength of
25 600 – 700 nm) within tumor tissue is less than 1.5 cm. Furthermore, the effective depth of the expected fluence zones is substantially less than the maximum, depending upon a number of factors such as the blood concentration in the tissue, color of the tissue, the photoreactive agent concentration, etc.

In conventional PDT, light at relatively high intensity is delivered to a
30 treatment site within a tumor through one or more optical fibers for a relatively short period of time, typically much less than one hour. In the prior art, the effect of the PDT is believed to be limited to the expected fluence zones, i.e., to the volume of the tumor directly illuminated by the light emitted from the optical fiber(s). In contrast, in the exemplary arrangement of optical fibers shown in
35 FIGURES 1 and 2, a relatively lower intensity light is provided from laser light source 26 at the distal end of each of optical fibers 30a-30e, and the light therapy

extends for a period of time greater than three hours – up to several days in duration. During this extended period of light therapy, additional photoreactive agent may be administered to the patient, depending upon the size of the tumor, the type of photoreactive agent used, and other conditions unique to each patient.

5 By administering lower intensity light for an extended period of time in this manner, the light therapy has been found to destroy a much larger volume than expected. Based on the teaching of the prior art, only abnormal tissue that has absorbed the photoreactive agent and has been directly illuminated by light emitted by each of the optical fibers within their expected fluence zones should be
10 destroyed by the PDT. As a result of the extended period of treatment using the plurality of optical fibers shown in FIGURES 1 and 2, a substantially expanded necrotic zone 38 in tumor 22 should be achieved in which the abnormal tissue well outside the expected fluence zones of each of the optical fibers is destroyed. The substantially greater volume of necrotic zone 38 in tumor 22 is believed to be
15 due to one or more causes that are concomitant to the destruction of abnormal tissue by conventional PDT achieved during a conventional short-term light therapy.

It is believed that the abnormal tissue outside the expected fluence zones around each optical fiber is destroyed due to one or more other factors or
20 processes that differ from the process involved in conventional short-term PDT. The extended duration PDT of the present invention is believed to cause an inflammation of the damaged abnormal tissue in the expected fluence zone, which then gives rise to the augmentation of a natural immune response of the patient's body. The natural immune response then destroys the abnormal tissue outside
25 expected fluence zones 36. While an immune response by the patient's body prior to the onset of the extended period of light therapy is not triggered by the presence of abnormal tissue in tumor 22, it is believed that the extended period of light therapy administered under the present invention may trigger inflammation and the immune response of the patient so that the abnormal tissue outside the
30 expected fluence zones is attacked and destroyed by the patient's own system.

Another possible cause for the expanded volume in which necrosis of the abnormal tissue in tumor 22 will occur in connection with the present invention is the oxygen depletion outside the expected fluence zones that arises due to the generation of singlet oxygen as light is administered to tumor 22 through the
35 optical fibers. Since the light is administered for an extended period of time, the conversion of molecular oxygen into singlet oxygen continues to occur during the

duration of the treatment, contrary to the teaching of the prior art, as more molecular oxygen diffuses into the expected fluence zones. The conversion of molecular oxygen that proceeds during the extended administration of light therapy depletes the oxygen available to the abnormal tissue outside the expected fluence zones, causing a gradient of hypoxia and anoxia in the portion of the tumor that is not directly illuminated by light. This continuing photodynamic transformation of molecular oxygen to singlet oxygen by the excited photoreactive agent within the expected fluence zones thus has an effect that expands outside those zones. In addition, it is possible that singlet oxygen produced in the expected fluence zones diffuses or circulates into the larger volume of the tumor outside these zones.

Another possible cause of the expanded necrotic zone achieved by the present invention is the spread of activated photoreactive agent from within the expected fluence zones into other portions of the tumor outside these zones. Once activated by light administered during the extended period of light therapy, the photoreactive agent diffuses and circulates outside the expected fluence zones and into other portions of the tumor, where it may destroy abnormal tissue. It is believed that the photoreactive agent that has been activated during the extended period of light therapy may itself have a destructive effect on abnormal tissue that subsequently absorbs it, and that this destructive effect is not oxygen dependent. The prior art has taught that the conversion of molecular oxygen to singlet oxygen is the primary cause of the destruction of abnormal tissue arising from conventional PDT, and that this conversion occurs only during a brief interval at the onset of the light therapy administration. However, the present invention achieves a substantially greater destruction of abnormal tissue over a substantially longer period of time than should be possible if this teaching of the prior art were correct. Thus, the present invention achieves an unexpected result that the prior art has taught should not be possible.

A further possible cause of the expanded necrotic zone obtained with the present invention is a vascular stasis, collapse, or occlusion occurring outside the expected fluence zones, due to any of the other concomitant factors discussed above, or due to any venous injury and thrombosis occurring within the expected fluence zones that propagate outside those zones. The vascular stasis, collapse, and occlusion occurring as a result of venous injury is known in the medical art, but has not previously been observed or disclosed as giving rise to an expanded volume of necrosis in a tumor following an extended period of light therapy.

There is another possible explanation for the much larger volume of abnormal tissue destroyed in accord with the present invention. Light applied to the abnormal tissue in the tumor is likely to be scattered along random paths within the tissue that may penetrate to a substantially greater depth within tissue, although at very much attenuated intensity. Accordingly, it may be that the expected fluence zone, which represents the limit of direct penetration of light, does not accurately define the full extent of the penetration of the scattered and reflected light within the abnormal tissue. This scattered and reflected light may be of too low an intensity to have much effect when administered for the relatively short duration of a conventional PDT procedure, but may have a much more pronounced effect when delivered for the extended duration of the present invention, so that the conversion of molecular oxygen to singlet oxygen occurs at a much greater depth within the tumor than the expected fluence zone would indicate.

The present invention is clearly not limited to administering light for an extended period of time using a laser source. Instead, almost any source of light can be used that emits light in the appropriate waveband, i.e., corresponding to the absorption waveband of the photoreactive agent. For example, the light source may comprise an electroluminescent device, an LED, a fluorescent light source, an incandescent light source, an arc lamp, or other source of light that is conveyed to a tumor through an optical fiber (or light pipe), or is disposed on a probe that is inserted into the tumor. Since the light is administered to the tumor for an extended period of time, it is generally preferable to implant the source of the light directly into the tumor at a plurality of sites and to energize the light sources with an electrical current from a power supply that is internal to the patient's body. It is undesirable for optical fibers or power leads to extend through the dermal layer of a patient's body for an extended period of time, since such practices are known to create a potential increased risk of infection. Instead, probes or light bars having a plurality of LEDs or other light sources disposed therein are preferably implanted within the tumor and energized using an implanted power source. An implanted conductive coil can be energized by electromagnetically coupling power across the dermal layer from an external coil connected to an alternating current source, or by otherwise producing a varying electromagnetic field outside the patient's body that is coupled to the implanted coil. U.S. Patent No. 5,715,837, which is assigned to the same assignee as the present invention,

discloses details of apparatus useful for this purpose, and its disclosure and drawings are hereby specifically incorporated herein by reference.

FIGURE 3 illustrates implanted probes 50a-50e, which have been inserted into tumor 22 in a generally circular pattern. As shown more clearly in
5 FIGURE 4, each of probes 50a-50e has a generally elliptical expected fluence zone 52, since the light is emitted from opposite sides of each probe and is not uniformly constant in a radial direction around the longitudinal axis of the probes. As shown in FIGURE 4, the expected fluence zones of probes 50a-50e generally overlap, forming a rough circle that encompasses or surround a central zone 56,
10 which does not receive any direct light emitted by the probes. Although conventional short-term PDT would destroy the abnormal tissue within expected fluence zones 52, the present invention provides for administering the light therapy for a much longer or extended period of time that enables abnormal tissue in a substantially larger volume comprising necrotic zone 38 of tumor 22 to be
15 destroyed. Necrotic zone 38 includes central zone 56, which is surrounded by expected fluence zones 52. Each of probes 50a-50e is coupled to the remote power source (not shown) through leads 54. The remote power source can comprise a battery or storage capacitor which store sufficient energy to provide the relatively low intensity light emitted by each of light probes 50a-50e, and/or
20 may comprise an implanted coil that receives electromagnetic energy from an external source (neither shown), as noted above.

Another aspect of the present invention arises from positioning the probes in a pattern such as that shown in FIGURES 3 and 4. This aspect of the present invention relates to the effect on central zone 56 of the necrosis of abnormal tissue
25 occurring in expected fluence zones 52 due to PDT. Since these expected fluence zones substantially surround central zone 56, all of the blood vessels that supply oxygenated blood to the central zone pass through these zones. The destruction in the expected fluence zones of blood vessels supplying oxygenated blood to central zone 56 should cause abnormal tissue within central zone 56 to be destroyed due
30 to oxygen and nutrient starvation. However, since the present invention will produce necrotic zone 38 that extends radially outward of the expected fluence zones, the present invention is not limited to a pattern of light probes (or optical fibers) that produce expected fluence zones overlapping to surround a central zone.

35 In FIGURE 5A, details of a probe 60 suitable for use in the present invention are illustrated. Probe 60 includes a flexible substrate 62 on which are

mounted a plurality of spaced-apart LEDs 66. Leads 64 are coupled to conductive traces (not shown) on flexible substrate 62 and provide electrical current to energize LEDs 66, causing them to emit a light 40 of the appropriate waveband within the light absorption waveband of the photoreactive agent. An optically transparent, biocompatible envelope 68 surrounds LEDs 66 and flexible substrate 62, sealing the structure so that the internal components are not exposed to bodily fluids.

FIGURES 5B and 5C illustrate details of probes 70 and 80, respectively, in which LEDs 66 are also used to emit light. However, in probe 70, lenses 72 are applied over LEDs 66 to focus light rays 40', minimizing the spread of the light emitted by each of the LEDs. In FIGURE 5C, concave mirrors 82 are mounted under LEDs 66, also focusing light 40'. Optically transparent, biocompatible envelopes 74 enclose each of probes 70 and 80, providing the same protection against bodily fluids as noted above in connection with envelope 68 of probe 60. By focusing the light emitted by LEDs 66, a more directed pattern defining the elongate shape of expected fluence zones 52 can be achieved with probes 70 and 80.

FIGURES 6A and 6B illustrate optical fibers 90 and 98, in which a distal portion of a core 94 exposed by removing a portion of cladding 92 limits the direction in which light rays 96 are emitted. In optical fiber 90, cladding 92 is removed around approximately one-half the circumference of core 94, adjacent the distal end of the optical fiber, so that light conveyed by the optical fiber is emitted only through the exposed surface of the core and through its end. In optical fiber 98, cladding 92 is removed from the entire portion of the distal end, and a hemispherical mirror coating 100 surrounds approximately one-half of the circumference of the exposed core. Light is thereby reflected from hemispherical mirror surface 100 through the exposed side of core 94. FIGURE 7 illustrates a cross-sectional view showing an expected fluence zone 110 extending approximately 1.5 centimeters, and a depth of tumor necrosis 112 that is greater than five centimeters in accord with the present invention. Optical fibers 90 and 98 permit light to be administered in a desired direction during the administration of an extended light therapy. For example, by using either of optical fibers 90 or 98, light can be directed toward the interior of a tumor, and light directed toward the periphery of the tumor can be minimized, thereby avoiding exposure of normal tissue outside the limits of the tumor to the light. The directional emission of light from optical fibers 90 and 98 can also be used to

define many different desired patterns for administering light therapy during the extended period in accord with the present invention.

With reference to FIGURE 8, a tumor 120 is illustrated in a plan view; a plurality of probes 122 that emit light of an appropriate waveband have been
5 implanted in spaced-apart array within the tumor, generally defining a circle. Each of probes 122 includes two separately energizable groups of light sources that emit light in opposite directions. Specifically, when light sources 124a are energized, light rays 126 are emitted that are generally directed toward the perimeter or periphery of tumor 120. As a further aspect of the present invention,
10 it is contemplated that by initially administering light rays 126 directed towards the periphery of the tumor, destruction of the abnormal tissue comprising tumor 120 will occur first around the periphery of the tumor. Thereafter, light sources 124b are energized, and light sources 124a are de-energized. Light sources 124b emit light rays 128 that are directed toward the inner portion of
15 tumor 120. Necrosis of the abnormal tissue around the periphery of the tumor should tend to cause vascular stasis, collapse, or occlusion of the vascular structure providing oxygenated blood to the inner portion of tumor 120. Accordingly, the extended light therapy provided by light rays 128 should continue the destruction of abnormal tissue within the interior of tumor 120 and
20 the actual necrotic zone will be extended as a result of one or more of the concomitant factors discussed above. An enhanced necrosis volume within tumor 120 is thus achieved using this two pronged light therapy. As a further benefit, less electrical current is required by each of probes 122, since only a portion of the light sources on each probe are energized at a given time. This
25 reduced electrical current thereby minimizes the capacity of the power source required to energize the probes.

FIGURE 9 illustrates a circuit 140 that can be used to selectively energize either light sources 124a or 124b. In this embodiment, the light sources comprise LEDs that only emit light when energized by the proper polarity voltage.
30 Circuit 140 includes a source 142 that supplies an alternating current through conductors 144 and 146. Conductor 144 is coupled to the anode of a silicon controlled rectifier (SCR) 148, to the cathode of an SCR 150, and through a conductor 152 to the cathode of an SCR 154, and the anode of an SCR 156. Similarly, conductor 146 is connected to the anode of an SCR 158, the cathode of
35 an SCR 160, and through a conductor 162, to the cathode of an SCR 164 and the anode of an SCR 166. The cathode of SCR 148, the anode of SCR 154, the

cathode of SCR 158, and the anode of SCR 164 are coupled through conductors 168 and 172 to the anode of the LEDs comprising first set of light sources 124a and to the cathode of the LEDs comprising second set of light sources 124b. Similarly, the anode of SCR 150, the cathode of SCR 156, the anode of SCR 160, and the cathode of SCR 166 are coupled through conductors 170 and 174 to the cathode of the LEDs comprising the first set of light sources 124a and the anode of the LEDs comprising the second set of light sources 124b. By selectively gating either SCRs 148, 150, 158, and 160 or SCRs 154, 156, 164, and 166, either first set of light sources 124a or second set of light sources 124b are selectively energized. The gating signal can be transmitted as an RF signal that is received and amplified before application to circuit 140, since the circuit is internally implanted within the patient's body. AC power source 142 can be an internally implanted coil, electromagnetically coupled to an external source of power, as noted above.

FIGURE 10 illustrates tumor 120 in which probes 180 are inserted generally in a radial direction within the tumor. Probes 180 each include a first set of LEDs 186 that are disposed adjacent an outwardly extending lead 182 of the probe, and a second set of LEDs 188 mounted on a flexible substrate 184 adjacent its inwardly extending distal end. A biocompatible, optically transparent envelope 190 encloses each of probes 180. Initially, first LEDs 186 are energized using circuit 140 so that light rays 192 are emitted from each of probes 180 in the region radially closer to a perimeter 130 of tumor 120. After the photoreactive agent absorbed by tumor 120 has been activated to destroy abnormal tissue adjacent the periphery of the tumor, first set of LEDs 186 are de-energized, and second set of LEDs 188 are energized, emitting light rays 194, which are incident on the inner portion of tumor 120. The concomitant factors occurring as a result of the extended duration of light therapy provided by light rays 192 and 194 thereby destroy substantially all of tumor 120, even though the total volume of tumor 120 is substantially greater than the expected fluence zone for the light sources on probes 180.

The discovery of the present invention arose in connection with an actual *in vivo* clinical test on a patient to treat a retroperitoneal tumor 200, generally shaped as shown in FIGURES 11A and 11B. Tumor 200 had been treated previously with chemotherapy and with radiation therapy. Also, attempts had been made to surgically remove it, but tumor 200 had been resistant to each of these conventional forms of treatment. In fact, at the time the clinical study was

undertaken, tumor 200 had grown through a dermal layer 202 so that a protruding portion 204 was exposed. In this clinical study, four light bars or probes 206 and two probes 208 were initially inserted into protruding portion 204 of the tumor. Since this portion of the tumor was fully exposed, it was not necessary to surgically or endoscopically implant probes 206 and 208, and the probes could be energized using electrical current from an external power supply 212 supplied through leads 210. The power supplied to produce light at each probe ranged between 25 and 35 mW. The probes were inserted into protruding portion 204 in the pattern illustrated in FIGURE 11B. The photoreactive agent aminolevulinic acid (ALA) was administered to the patient approximately five hours prior to energizing probes 206 and 208. Probes 208 were inadvertently pulled from the tumor and were de-activated after approximately 18 hours, leaving the remaining four probes 206 in place and activated for a total of 48 hours.

Four weeks following the administration of the extended light therapy to tumor 200, necrosis in the protruding portion was observed up to approximately five centimeters away from the point where the nearest probe had been disposed. The maximum depth of the necrosis within protruding portion 204 was 5 cm beyond the distal tip of any of the probes. Thus, the extent of the necrosis observed in tumor 200 was substantially and unexpectedly greater than would have been expected based upon the teachings of the prior art. This extensive volume of necrosis is believed to have been caused by one or more of the concomitant factors discussed above. The substantially greater volume of necrosis, extending both radially and in depth well beyond the expected fluence zones of the probes, far exceeds that which would have been expected based upon PDT destruction of the abnormal tissue directly illuminated by light from probes 206 and 208 in these zones.

FIGURES 12 and 13 illustrate two further exemplary configurations for placing probes within a tumor 220. In these exemplary configurations, the abnormal tissue comprising the tumor is treated with an appropriate photoreactive agent prior to administration of the extended light therapy. In FIGURE 12, probes 222a, 222b, and 222c are angled inwardly so their outwardly extending proximal ends are radially further apart than their inwardly extending distal ends. A probe 222d is inserted generally within the central region of tumor 220, adjacent its upper surface. Leads 224 extend from the probes to a remote power source (not shown) for energizing the probes so that they emit light into the tumor. By positioning probe 222d transversely within the central portion of the tumor, the

light pattern provided by the probes should enhance the volume of necrosis resulting from one or more of the concomitant factors discussed above. The interior of tumor 220 should be deprived of oxygen due to the destruction of the vascular system surrounding it and this factor should also enhance the destruction of abnormal tissue resulting from the extended light therapy.

A similar result is achieved using the exemplary configuration of probes 226a-226e within tumor 220 shown in FIGURE 13. Again, leads 224 couple these probes to a remote power source (not shown). In this embodiment, each of the probes are generally inserted into tumor 220 so that their longitudinal axes are generally parallel with each other. Probe 226c is inserted into the center of tumor 220 and includes light sources adjacent its proximal and distal ends that are energized to produce a fluence zone 228 and 230 as illustrated in FIGURE 13. The volume between fluence zones 228 and 230, which does not receive direct light from any of the probes, is nevertheless destroyed due to the vascular effects caused by destruction of the surrounding abnormal tissue. The oxygen and nutrient supply to the internal portion of tumor 220 is thus cut off due to the necrosis of the vascular system around the periphery of the tumor.

It will be apparent that the probes and leads in the above examples may be replaced with optical fibers coupled to one or more internal or external light sources. In addition, it should be apparent that many other configurations of probes or optical fibers can be employed to achieve the concomitant effects resulting from long-term administration of light therapy in accord with the present invention.

Although the present invention has been described in connection with the preferred forms of practicing it, those of ordinary skill in the art will understand that many other modifications can be made thereto within the scope of the claims that follow. Accordingly, it is not intended that the scope of the invention in any way be limited by the above description, but instead be determined entirely by reference to the claims that follow.

The invention in which an exclusive right is claimed is defined by the following:

1. A method for destroying abnormal tissue in a tumor within a patient's body using an extended light therapy and at least one concomitant effect thereof, comprising the steps of:

(a) administering a photoreactive agent to the abnormal tissue, said photoreactive agent being preferably absorbed by the abnormal tissue rather than by normal tissue in the patient's body and having a characteristic absorption waveband;

(b) administering light to a treatment zone in the tumor that is determined by the penetration depth of the light into the tumor along a direct path, said light having a waveband corresponding to the absorption waveband of the photoreactive agent, a pattern in which said light is administered to the tumor defining a shape of the treatment zone so that the treatment zone encompasses a substantial portion of the tumor not penetrated by the light being administered along a direct path and is thus outside the treatment zone; and

(c) continuing to administer the light to the treatment zone for at least three hours of extended light therapy, said light destroying the abnormal tissue that it illuminates by activating the photoreactive agent absorbed thereby, said extended period of light therapy indirectly destroying said substantial portion of the tumor that is not penetrated by the light being administered by inducing said at least one concomitant effect that destroys the abnormal tissue comprising said substantial portion of the tumor.

2. The method of Claim 1, wherein destruction of the abnormal tissue in the treatment zone deprives said substantial portion of the tumor from receiving oxygen, said abnormal tissue in said substantial tissue thus being destroyed due to oxygen depletion.

3. The method of Claim 1, wherein the photoreactive agent in the treatment zone that is activated by the light being administered thereto diffuses into said substantial portion of the tumor that is not penetrated by the light, said photoreactive agent that is thus activated being operative to destroy the abnormal tissue in the substantial portion of the tumor.

4. The method of Claim 1, wherein the light therapy causes necrosis of the abnormal tissue in the treatment zone, which causes one of an immune response and an inflammation in the patient's body that destroys the abnormal tissue in said substantial portion of the tumor.

5. The method of Claim 1, wherein destruction of abnormal tissue in the treatment zone causes one of vascular collapse, stasis, and occlusion, so that blood flow to said substantial portion of the tumor is interrupted, causing the abnormal tissue in said substantial portion to die.

6. The method of Claim 1, wherein the light is administered through an optical fiber from a source that is external to the patient's body.

7. The method of Claim 1, further comprising the step of implanting a plurality of probes for administering the light into the tumor at spaced-apart locations within the treatment zone to determine the shape of the treatment zone.

8. The method of Claim 7, wherein the light is administered from at least one light source included on each of the plurality of probes.

9. The method of Claim 7, wherein the light is delivered to the plurality of probes through a plurality of optical fibers from a source that is external to the patient's body.

10. The method of Claim 7, wherein the depth at which light from each of said plurality of probes penetrates the tumor in the treatment zone is not more than about 3 cm.

11. The method of Claim 1, wherein the light administered to the treatment zone produces singlet oxygen, which depletes oxygen from said substantial portion of the tumor, causing a gradient of a hypoxia and an anoxia in said substantial portion of the tumor that leads to a destruction of the abnormal tissue in said substantial portion of the tumor.

12. The method of Claim 7, further comprising the steps of:

- (a) emitting light into the tumor in a first direction from each of the plurality of probes, said first direction being determined relative to each probe from which the light is emitted and not necessarily identical for each probe;
- (b) terminating light emission into the tumor in the first direction; and
- (c) emitting light into the tumor in a second direction from each of the plurality of probes, said second direction being substantially different from the first direction for each of the probes from which the light is emitted.

13. The method of Claim 12, wherein the first direction is toward a perimeter of the tumor, and the second direction is toward an interior of the tumor, light emitted in the first direction causing destruction of the abnormal tissue toward the perimeter of the tumor from each probe, which improves an efficacy with which the light emitted in the second direction destroys the abnormal tissue.

14. A method for destroying abnormal tissue in a tumor within a patient's body using an extended light therapy that induces necrosis of the abnormal tissue beyond a zone over which the light therapy is administered, comprising the steps of:

- (a) administering a photoreactive agent to the abnormal tissue of the tumor, said photoreactive agent being preferentially absorbed by the abnormal tissue rather than by normal tissue in the patient's body and having a characteristic light absorption bandwidth;
- (b) administering light to the abnormal tissue at a plurality of spaced-apart sites within the tumor through a plurality of probes that are inserted within the tumor, light from said plurality of probes only penetrating the abnormal tissue within a treatment zone comprising a limited volume of the tumor, said light being within the characteristic light absorption bandwidth of the photoreactive agent, said light activating the photoreactive agent to destroy the abnormal tissue illuminated by the light by a process of photodynamic therapy; and
- (c) continuing the administration of light through the plurality of probes for an extended treatment period in excess of three hours, said extended treatment period inducing a secondary effect that causes necrosis of the abnormal tissue outside the treatment zone, in a region of the tumor that is not penetrated by the light traveling in a direct path.

15. The method of Claim 14, wherein the probes are inserted into the tumor in a pattern that at least partially surrounds said region of the tumor that is not penetrated by the light traveling in a direct path, destruction of the abnormal tissue in the treatment zone by the photodynamic therapy causing one of a vascular stasis, collapse, and occlusion that induces the necrosis of the abnormal tissue outside the treatment zone.

16. The method of Claim 14, further comprising the step of directing the light from the plurality of probes in a predefined direction to limit administration of the photodynamic therapy to a defined portion of the tumor.

17. The method of Claim 16, wherein the step of directing comprises the step of providing a reflective surface on one side of the probe to limit administration of the light in the predefined direction.

18. The method of Claim 14, wherein destruction of the abnormal tissue in the treatment zone due to the photodynamic therapy induced necrosis of the abnormal tissue outside the treatment zone due to one of an immune response and an inflammation.

19. The method of Claim 14, wherein the necrosis of the abnormal tissue outside the treatment zone is induced as a result of an oxygen depletion in said abnormal tissue caused by formation of singlet oxygen in the treatment zone during the extended treatment period.

20. The method of Claim 14, wherein the necrosis of the abnormal tissue outside the treatment zone occurs due to a diffusion and circulation of the photoreactive agent into said abnormal tissue following activation of said photoreactive agent by administration of the light to the treatment zone during the extended treatment period, the activation of said photoreactive agent by the light enabling it to destroy the abnormal tissue outside the treatment zone.

21. The method of Claim 14, wherein the plurality of probes emit light that is produced by at least one light source on each of the plurality of probes.

22. The method of Claim 14, wherein the plurality of probes are each coupled to a source of light that is external to the patient's body by a different one of a corresponding plurality of optical fibers.

23. The method of Claim 14, wherein a plurality of spaced-apart light sources are included within each of the plurality of probes.

24. The method of Claim 23, where different ones of the plurality of light sources on at least one of the plurality of probes are selectively energizable so that a first portion of the plurality of light sources that emit the light in a first predefined direction are energizable separate from a second portion of the plurality of light sources that emit light in a second predefined direction.

25. The method of Claim 14, wherein the plurality of probes are transcutaneously inserted into the tumor.

26. The method of Claim 25, further comprising the step of energizing the plurality of probes from an external source of power by transcutaneous transfer of energy.

27. The method of Claim 14, further comprising the step of alternating a direction in which the light is administered to the tumor from each probe between at least a first and a second direction during the extended treatment period, said first direction being substantially different than the second direction.

28. The method of Claim 27, wherein the light is only administered in one of the first and the second directions at a time.

AMENDED CLAIMS

[received by the International Bureau on 18 October 1999 (18.10.99);
original claim 1 amended; remaining claims unchanged (1 page)]

The invention in which an exclusive right is claimed is defined by the following:

1. A method for destroying abnormal tissue in a tumor within a patient's body using an extended light therapy and at least one concomitant effect thereof, comprising the steps of:

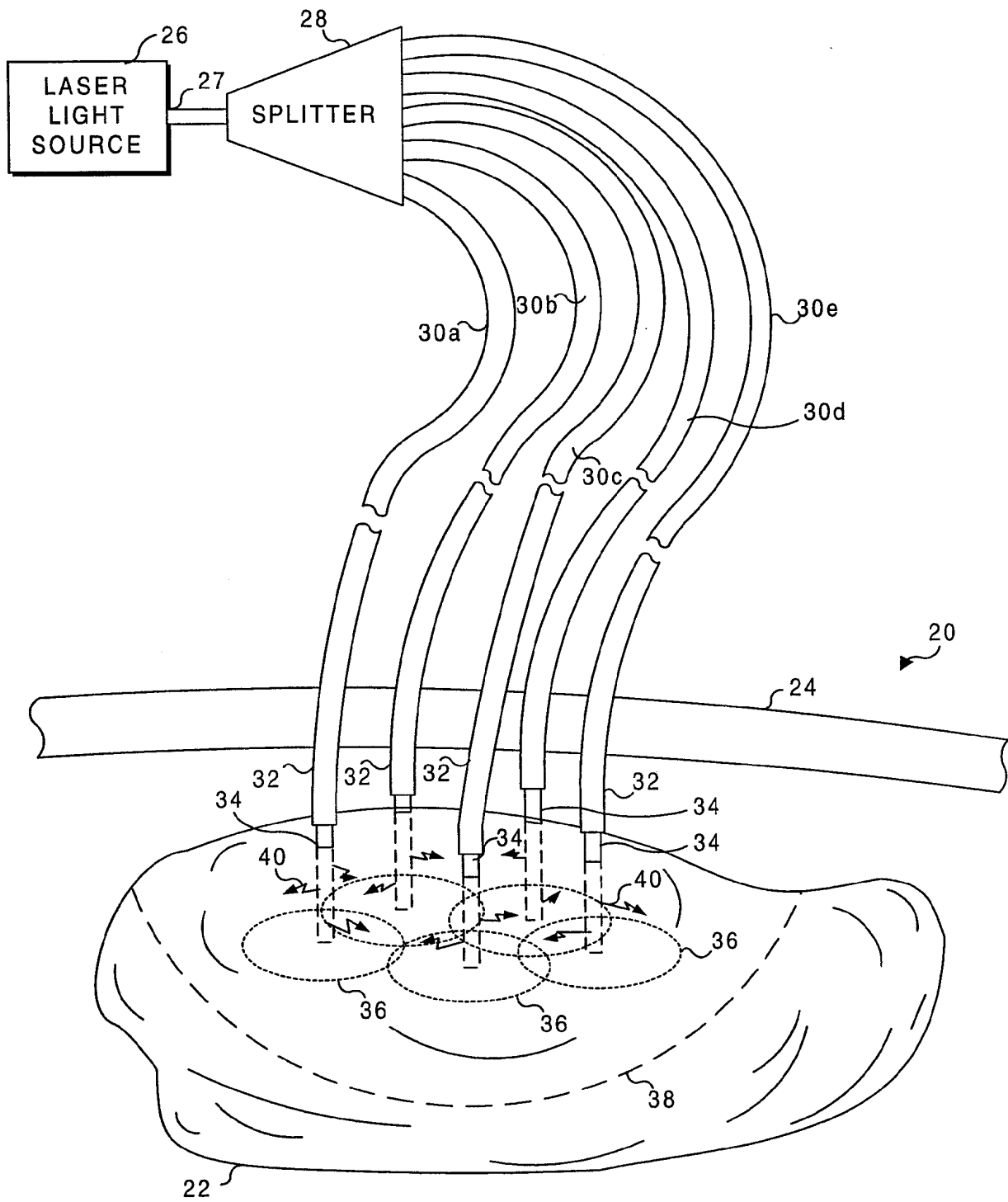
(a) administering a photoreactive agent to the abnormal tissue, said photoreactive agent being preferably absorbed by the abnormal tissue rather than by normal tissue in the patient's body and having a characteristic absorption waveband;

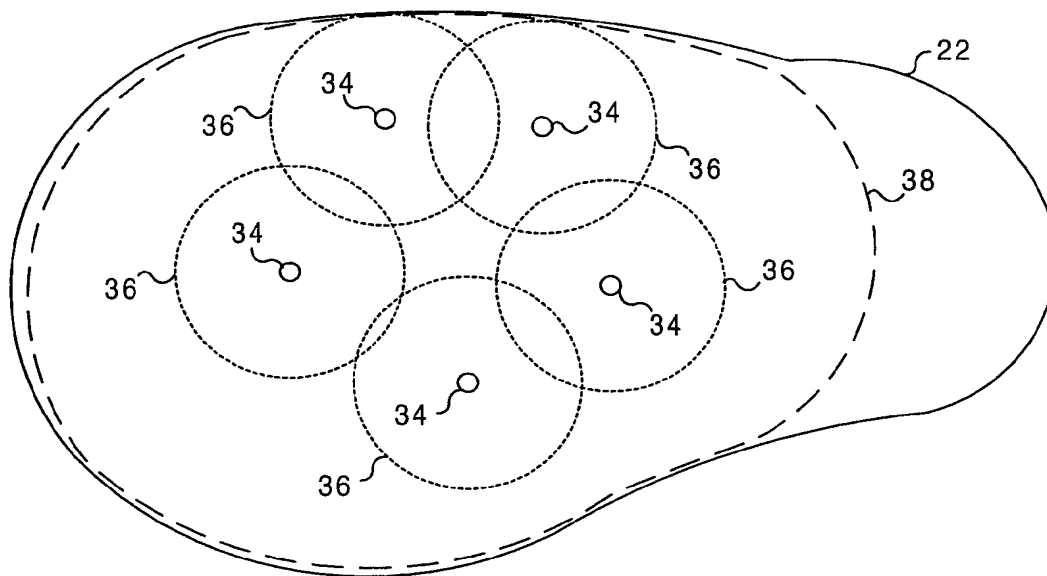
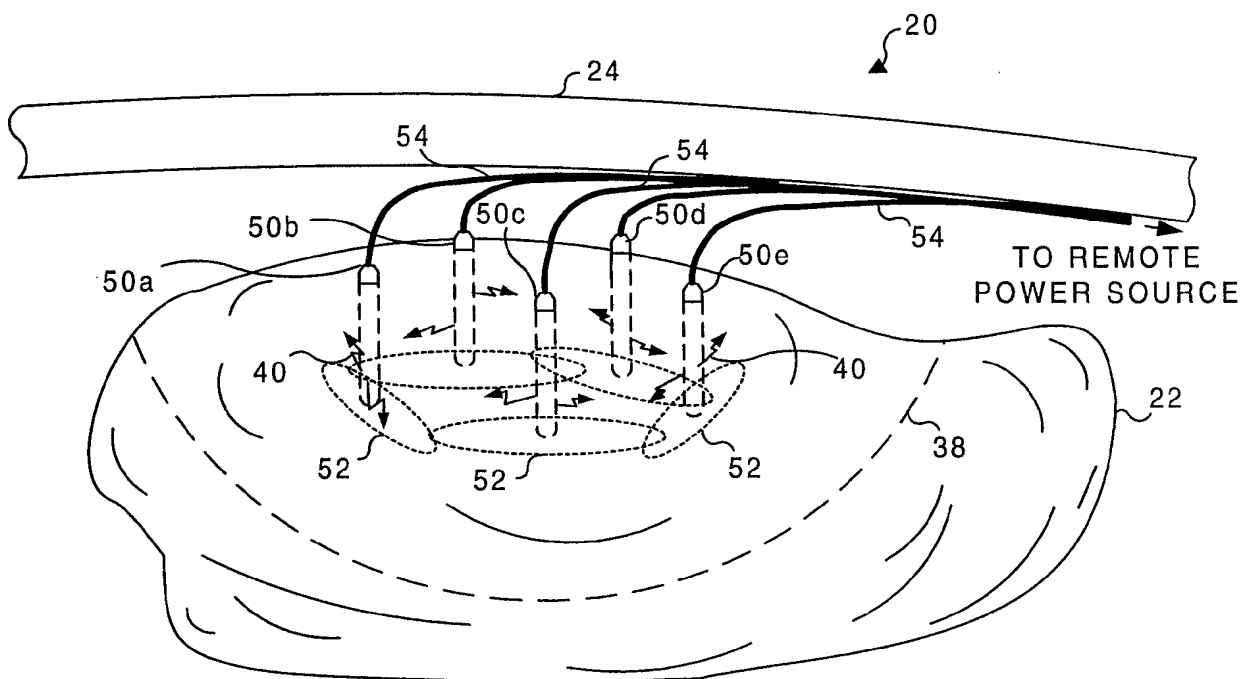
(b) administering light to a treatment zone in the tumor to a depth that is determined by the penetration depth of the light into the tumor along a direct path, said light having a waveband corresponding to the absorption waveband of the photoreactive agent, a pattern in which said light is administered to the tumor defining a shape of the treatment zone, the treatment zone encompassing a substantial portion of the tumor not penetrated by the light being administered along a direct path; and

(c) continuing to administer the light to the treatment zone for at least three hours of extended light therapy, said light destroying the abnormal tissue that it illuminates by activating the photoreactive agent absorbed thereby, said extended period of light therapy indirectly destroying said substantial portion of the tumor that is not penetrated by the light being administered by inducing said at least one concomitant effect that destroys the abnormal tissue comprising said substantial portion of the tumor.

2. The method of Claim 1, wherein destruction of the abnormal tissue in the treatment zone deprives said substantial portion of the tumor from receiving oxygen, said abnormal tissue in said substantial tissue thus being destroyed due to oxygen depletion.

3. The method of Claim 1, wherein the photoreactive agent in the treatment zone that is activated by the light being administered thereto diffuses into said substantial portion of the tumor that is not penetrated by the light, said photoreactive agent that is thus activated being operative to destroy the abnormal tissue in the substantial portion of the tumor.

**FIG. 1**

**FIG. 2****FIG. 3**

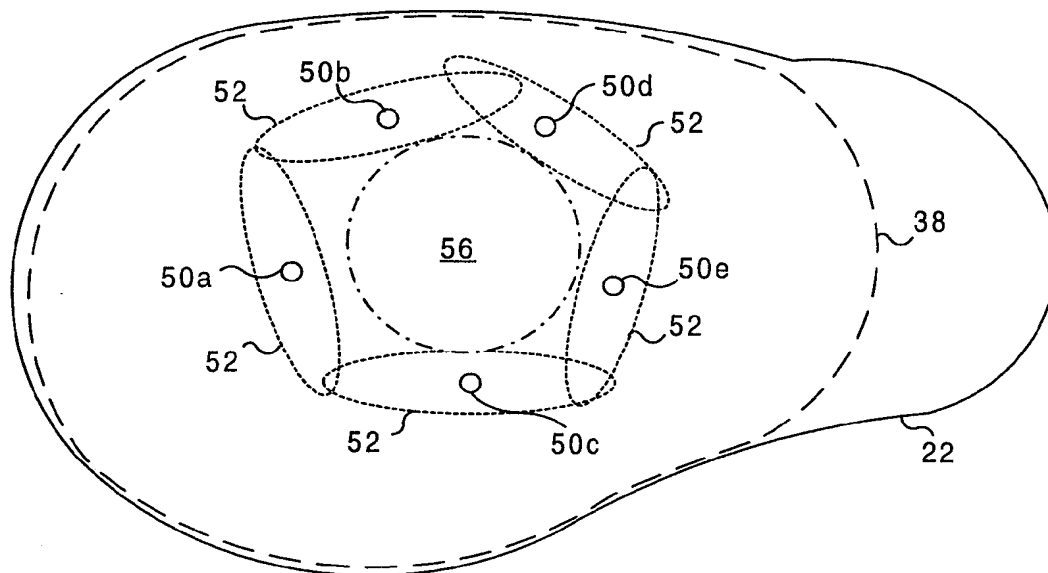


FIG. 4

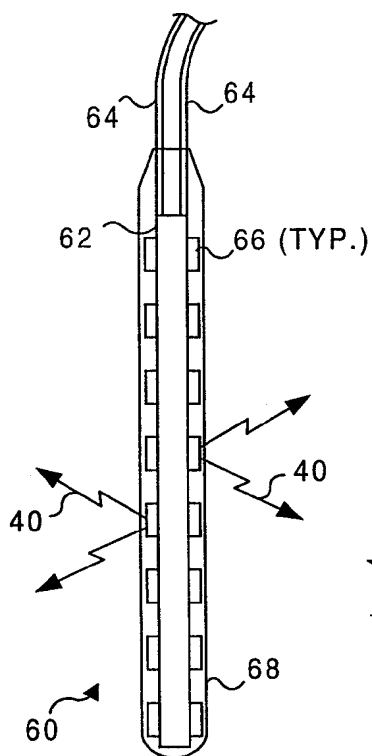


FIG. 5A

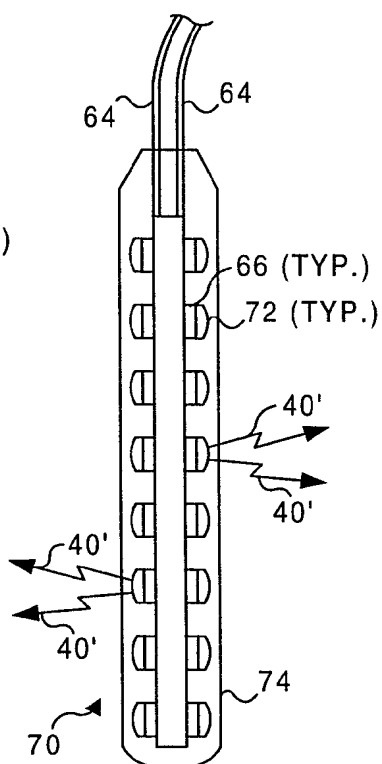


FIG. 5B

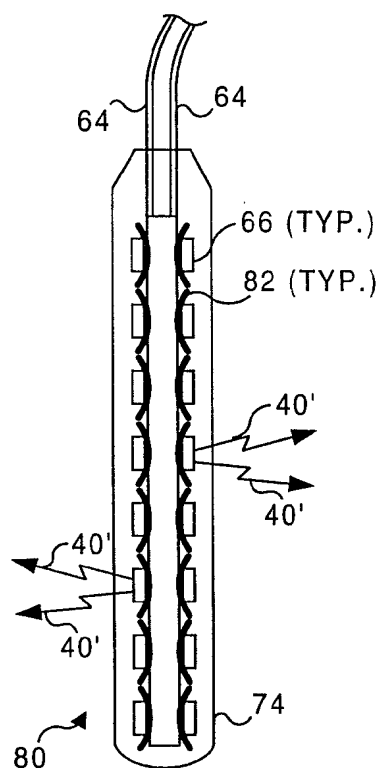


FIG. 5C

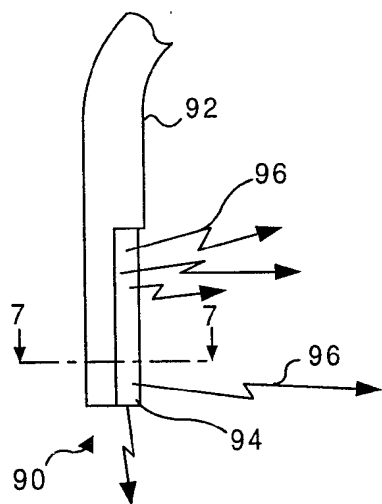


FIG. 6A

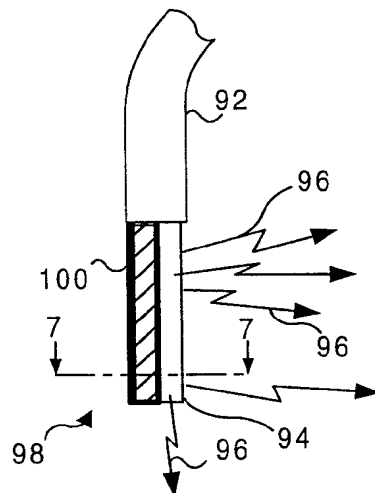


FIG. 6B

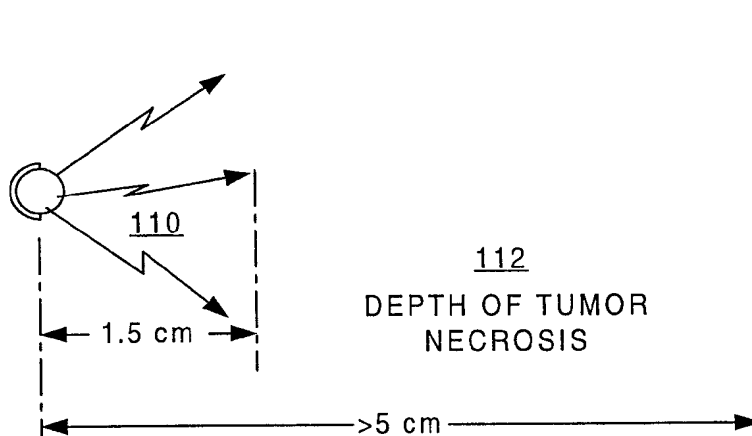


FIG. 7

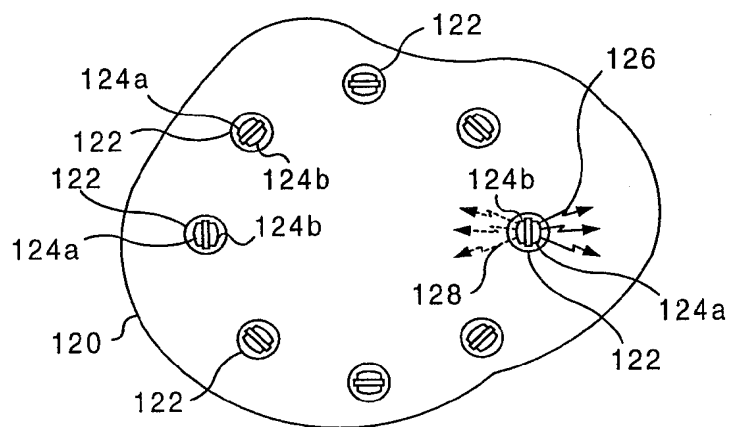
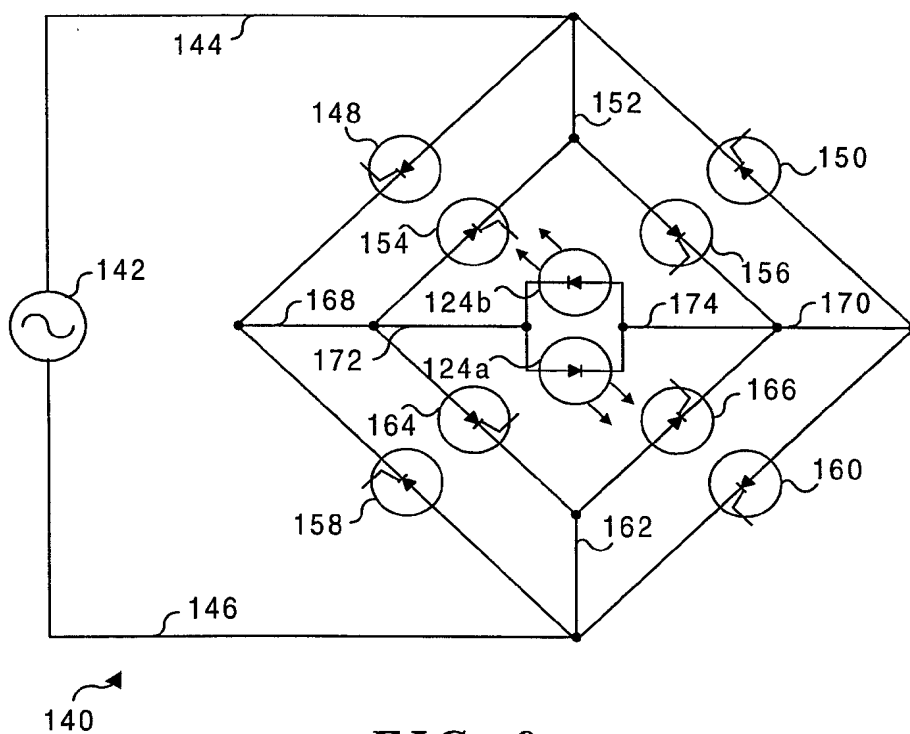
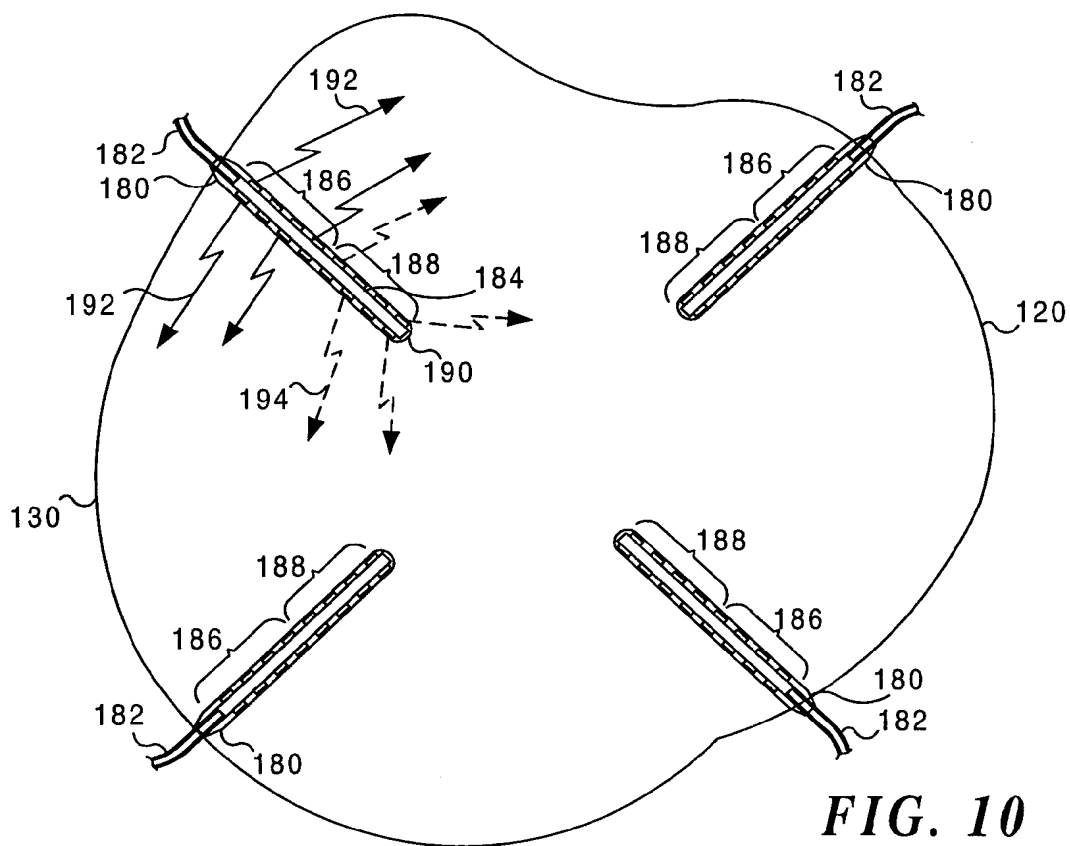


FIG. 8

**FIG. 9****FIG. 10**

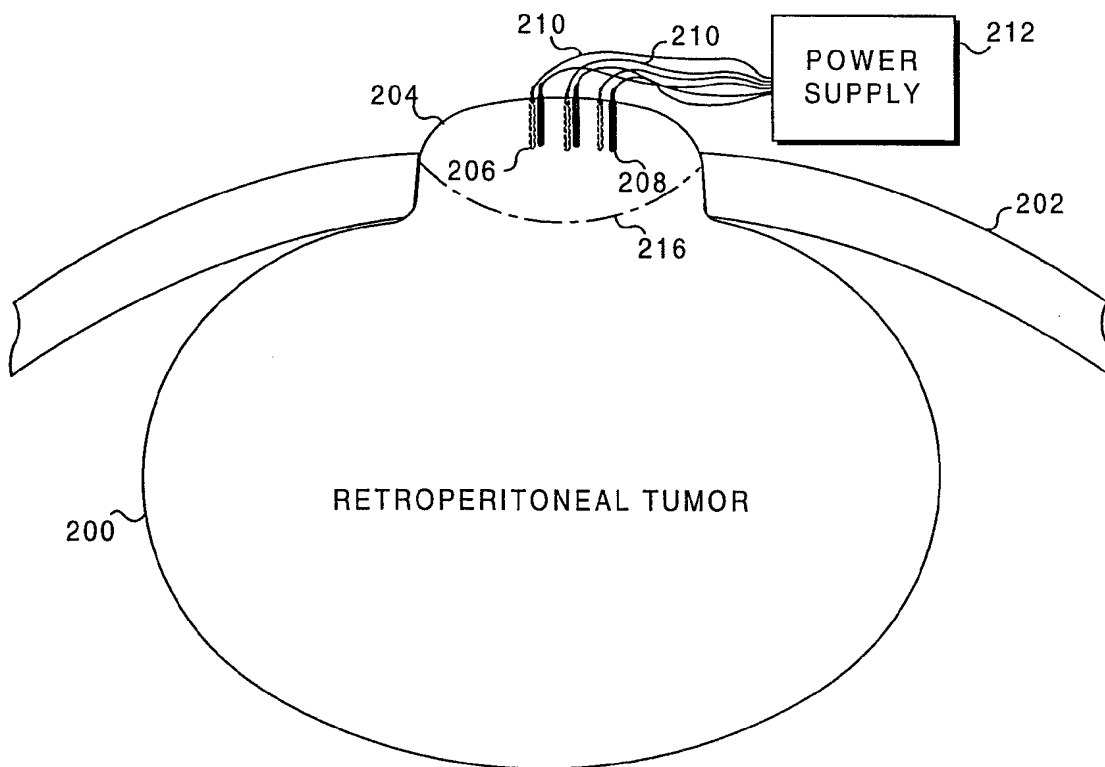


FIG. 11 A

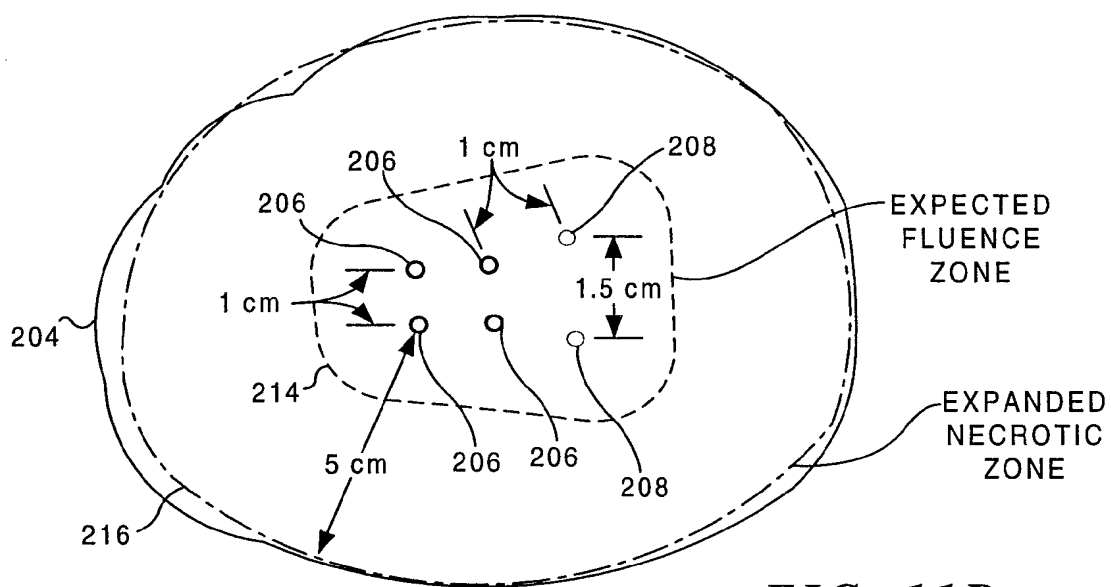


FIG. 11B

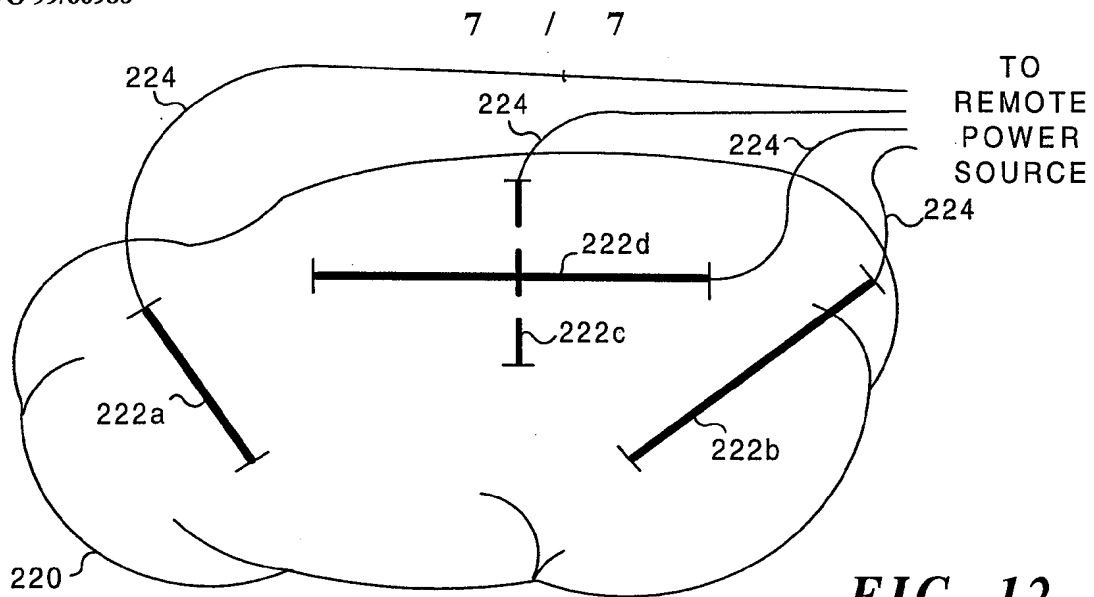


FIG. 12

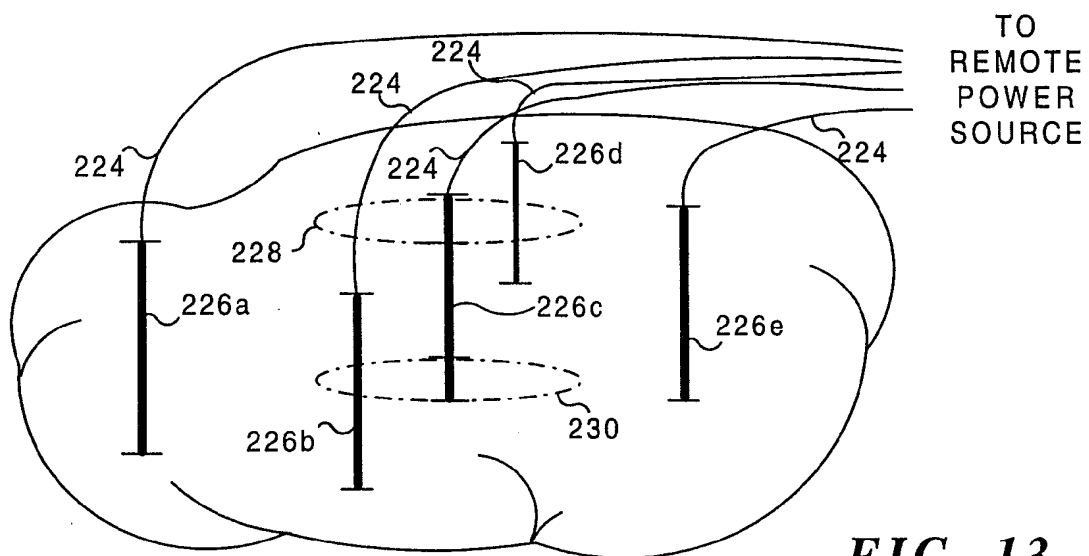


FIG. 13

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/09582**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(6) :A61N 5/06

US CL :607/88

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 606/3, 10-13, 15-18; 607/88-91, 93

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 4,336,809 A (CLARK) 29 June 1982, entire document.	14-28
Y	US 5,000,752 A (HOSKIN et al.) 19 March 1991, entire document.	14-28

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Further documents are listed in the continuation of Box C.

☐

See patent family annex.

* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
A document defining the general state of the art which is not considered to be of particular relevance	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
E earlier document published on or after the international filing date	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	* & * document member of the same patent family
O document referring to an oral disclosure, use, exhibition or other means	
P document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

22 AUGUST 1999

Date of mailing of the international search report

28 SEP 1999

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